

# American Journal of Obstetrics and Gynecology

VOL. 33

MAY, 1937

No. 5

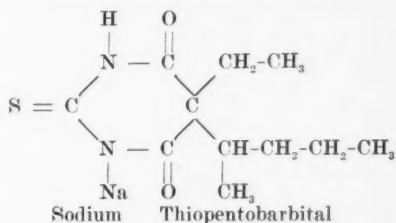
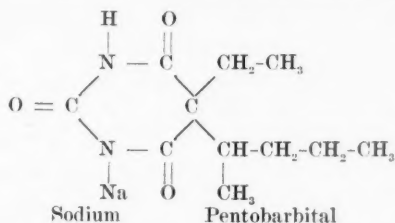
## Original Communications

### ON CERTAIN PHARMACOLOGIC ACTIONS OF THE NEWER BARBITURIC ACID COMPOUNDS\*

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THE clinical usefulness of the barbituric acid derivatives in obstetrics can best be evaluated and discussed by obstetricians who have had clinical experience with these drugs. Suffice it to say that some writers claim excellent, others unfavorable clinical results with the same drug.<sup>1</sup> Today the obstetrician is confronted not only by one but by many barbiturates and to make things more complicated a second series, the thioderivatives, have recently been introduced into medicine.<sup>2</sup> As we shall point out in this paper, the substitution of sulphur for the oxygen in the malonyl urea ring has changed the actions of the drug enormously.



All barbiturates when administered orally, rectally, intramuscularly, or intravenously produce varying stages of hypnosis, narcosis, or anesthesia and even death. The effect obtained is dependent not only upon

\*This investigation was made possible principally by a grant from Parke, Davis and Co., to the Jefferson Medical College for research in science.

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the amount of the drug administered but also upon the type of barbiturate given. In experimental animals barbital and phenobarbital produce anesthesia lasting from seven to thirteen hours, amytal two to seven hours, ortal and pentobarbital one to two hours, and evipal, thio-pentobarbital and thio-ethamyl only fifteen to thirty minutes. The duration of this effect can be modified by certain changes in the body. Hirschfelder and Haury<sup>3</sup> have shown that nephrectomy lengthens this action for phenobarbital and barbital from eleven to thirteen hours to thirty-six and seventy-nine hours, respectively. This operation has no effect upon the duration of action of amytal, pentobarbital, ortal, and evipal.

We<sup>4</sup> studied the effect of nephrectomy upon the duration of anesthesia produced by ortal sodium in dogs. In these there was no change. Liver damage, however, lengthens the actions of the short acting group. It is evident from these results that the effects of the former two drugs, since they are eliminated by the kidney, would be lengthened in nephritic patients, whereas the latter, amytal, ortal, etc., which are probably destroyed by the liver, would show increased duration of anesthesia in cases with liver damage. Recently some evidence has been presented to show that all barbiturates including amytal and pentobarbital are excreted by the kidneys.<sup>5</sup> This has been denied by others<sup>6</sup> who have shown that probably only degradation products appear in the urine following anesthetic doses of amytal, pentobarbital, and ortal.

The rapidity with which the latter drugs leave the circulation when injected intravenously was shown by Brundage and Gruber.<sup>7</sup> One to seven minutes after the intravenous injection of anesthetic doses of these drugs only 2 to 5 mg. per 100 c.c. of blood was observed, i.e., only about  $\frac{1}{10}$  of the amount injected intravenously remained in the entire circulation one to seven minutes after their injection. This level was maintained until the animal came out from under the anesthetic one to three hours later. This seems to show that these drugs are stored in some tissues of the body and for some time thereafter they are given back to the blood stream as fast as they are destroyed by the liver. The total amount of these degradation products excreted in the urine varies considerably with different barbiturates in different animals. In our investigation as small amounts as 2.4 to 7.5 per cent of the sodium salts of amytal and ortal may appear in the urine upon their intravenous injection. However, as much as 22 per cent of the sodium pentobarbital may be found in the urine during the same period. The substance excreted, however, as far as we could determine is not the barbiturate. The intraperitoneal injection of this excreted material into mice produces neither hypnosis nor anesthesia.

✓ One of the objectionable features of all barbiturates in obstetrics is the high percentage of cases showing extreme restlessness and maniacal symptoms. Some of these patients require restraint for delivery. Some clinicians report one-third of their patients markedly restless and one-



third moderately restless.<sup>8</sup> Ruth and Paxson<sup>9</sup> record this restlessness due to the use of amytal as a disadvantage. Similar objections were voiced by Bohler<sup>10</sup> and Olson and Van Ess<sup>11</sup> with the use of pernocton,



Fig. 1.—Dog, 11 kg. Light ether anesthesia. 1, Respiration with a pneumograph about the upper abdomen and the thorax. Down stroke is that of inspiration. 2, Blood pressure from the carotid artery taken with a mercury manometer using heparin as the anticoagulant. 3, Time in ten seconds and zero blood pressure. 4, Duration and time of injection of 600 mg. of sodium amytal intravenously. There are noted a marked fall in the general blood pressure and a decrease in the rate and depth of respiration, both returning to normal seventy-five minutes later.

and Galloway and Smith<sup>12</sup> and Boylan<sup>13</sup> with pentobarbital. Most obstetricians report the production of amnesia in the majority of patients treated with barbiturates.<sup>14</sup>

A corresponding period of excitement before the production of anesthesia is noted in experimental animals with amytal, pentobarbital,

ortal, evipal, and thiopentobarbital. In some animals evipal and thiopentobarbital do not produce narcosis but convulsions. In our studies<sup>15</sup> on rats, we employed a sudden mechanical stimulus to the tail instead of the slow pressure stimulus as outlined by Eddy<sup>16</sup> for eliciting the degree of anesthesia. In these, evipal and thiopentobarbital did not abolish reflexes unless morphine sulphate was added. In some animals, evipal was administered in toxic doses, yet the animal responded by a sudden contraction of the skeletal muscles upon sudden pressure applied to the tail, ear, or foot. We were also unable to produce anesthesia in the majority of the rabbits studied upon the intravenous injection of evipal and thiopentobarbital. Cessation of respiration usually occurred before anesthesia could be produced.

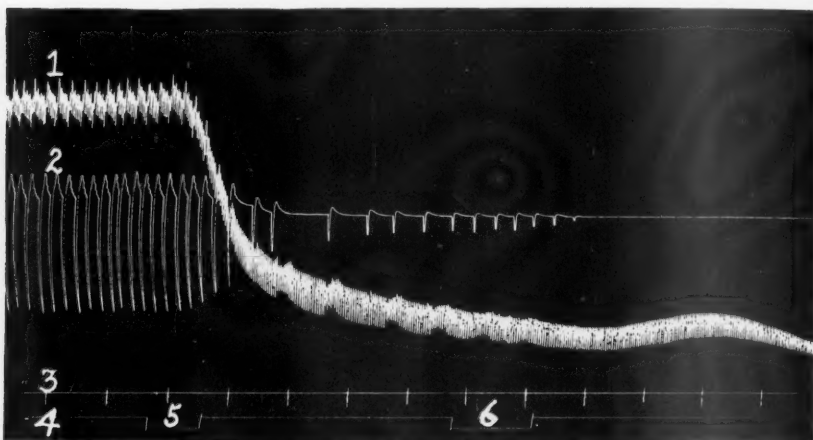


Fig. 2.—Dog, 9.5 kg. Paraldehyde anesthesia. 1, Blood pressure with mercury manometer. 2, Respirations recorded with pneumograph. Down stroke in the record is that of inspiration. 3, Time in fifteen seconds and writing point at atmospheric pressure. 4, Duration and time of injection of 400 mg. of sodium phenobarbital intravenously (at 5). Caffeine sodiobenzoate injected (at 6). Record shows complete cessation of respiration before the heart ceased beating.

In addition to hypnosis and anesthesia all of these drugs depress the respiratory center and death may result<sup>17</sup> (see Figs. 1 and 2). Since the respiratory center is affected before the cardiovascular system, there is always a possibility of using artificial respiration and thus preventing a catastrophe.

It has been shown in pregnant dogs<sup>18</sup> and rats<sup>19</sup> that these drugs pass freely from the mother through the placenta to the fetus and back again into the mother's circulation. Jaroschka<sup>20</sup> found barbiturate in the urine of two dead fetuses following the use of pernocton in the delivery of the mothers. It is apparent, therefore, that infants born of mothers under deep barbiturate anesthesia may show some difficulty in establishing spontaneous respiration.<sup>21</sup> Some authors report one-third of the babies as apneic at birth with difficult resuscitation. Others cite even stillbirths. Averett<sup>22</sup> reports the fact that in his series, 8 babies required resuscitation, upon the use of nembutal and scopolamine in the mothers. Bohler<sup>10</sup> reports 3 babies narcotized following the use of pernocton in 102 obstetric cases, and Galloway

and Smith<sup>12</sup> report 31 babies as being blue and 9 pallid in their series of 500 cases with the use of nembutal (pentobarbital) and scopolamine as the anesthetic in delivering the mothers. With the use of dial in 143 obstetric cases, Bernberg and Livingston<sup>8</sup> noted 8 infants lightly, 8 moderately, and 15 markedly narcotized, a total of 31 cases or 21 per cent of the babies born in their series.

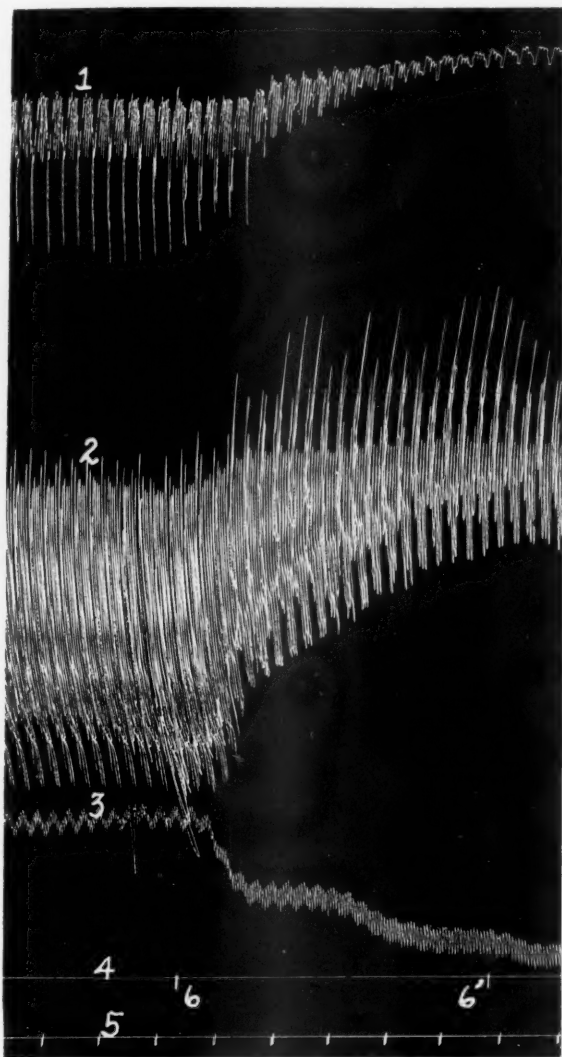


Fig. 3.—Dog, 29 kg. Ether anesthesia. 1, Auricular contractions. 2, Ventricular contractions recorded with a Cushny myocardiograph. 3, Blood pressure taken from carotid artery with mercury manometer. Heparin used as anticoagulant. 4, Point of injection. 5, Time in intervals of ten seconds and zero blood pressure. Between 6 and 6', 580 mg. sodium pentobarbital were injected intravenously.

The second source of danger is the effect on the cardiovascular system. Many investigators totally ignore this fact. It should be pointed out that all of these drugs depress the heart muscle. In experimental animals the heart dilates and the contractions become weaker as shown by

the Cushny myocardiograph<sup>23</sup> applied to the heart (Fig. 3) and by experiments with perfused excised hearts.<sup>24</sup> Complete cessation of contraction of the excised monkey's heart when perfused with evipal was shown by Storm. All of the ordinary barbiturates depress the peripheral vagus nerve endings, and a stronger stimulus is required to inhibit the heart. This is readily shown upon electrical excitation of

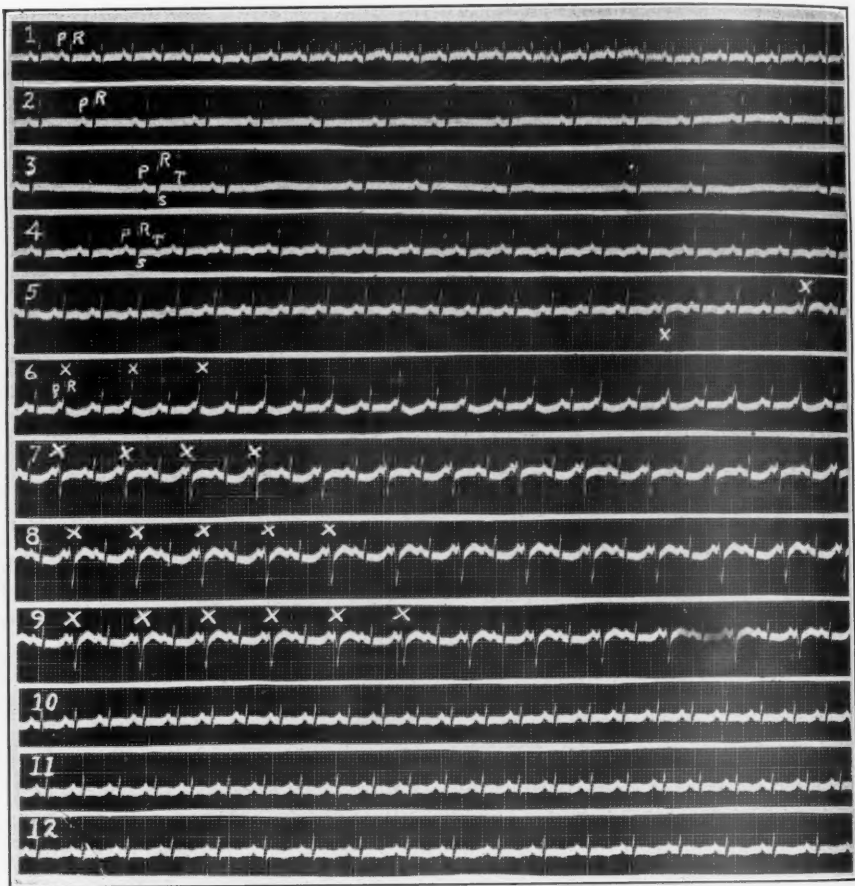


Fig. 4.—An electrocardiogram taken in a dog weighing 11.8 kg. Records taken before and after injections of morphine sulphate and sodium pentothal. Lead II. 1 mv. = 1 cm. Res. 2000 ohms. Controls 1 and 2. Record 1 was taken during a period of playful excitement and 2, five minutes later after the animal had become quiet. The animal was then given 5 mg. per kg. of morphine sulphate subcutaneously. Record 3 was taken fifty-four minutes after the injection of morphine. Sixty-two minutes after the injection of morphine 236 mg. of pentothal sodium (20 mg. per kg.) were injected intravenously. Duration of injection was four and one-half minutes. The respirations were good throughout the experiment. Record 4 was taken two minutes after the beginning of the injection of pentothal and Record 5 at the close. Number 6 was taken one minute later and 7 and 8, two and two and a half minutes, respectively, after the end of the administration. Number 9, three; 10, four; 11, six; and 12, fourteen minutes after the injection. Duration of anesthesia which was difficult to determine because of the morphine was approximately one hour. P-R interval: Normal 3/25 sec.; after morphine sulphate 4/25 sec.; and after pentothal sodium 1/10 sec. Alternate normal and premature contractions are noted near the end of Record 5 at x, and can be seen in Records 6, 7, 8, and 9 at x. T-wave becomes inverted after the injection of pentothal sodium. Cardiac rates are: normal at 100; after morphine sulphate 60; and after pentothal sodium 190 beats per minute.

the vagus in dogs and cats under amytal,<sup>25</sup> pentobarbital,<sup>26</sup> oral and evipal<sup>27</sup> anesthesia. The increase in the maternal and fetal heart rates in obstetric cases may be due in part to such an effect. The thioderivatives, however, increase the responsiveness of the heart to the vagus stimulation. Vagus excitation with the same strength of current following thiopentobarbital, thio-ethamyl, and pentothal administration produces greater inhibition of the heart, and in some cases the slowing of the heart is changed to complete stoppage following such excitation.<sup>27</sup> It should also be pointed out that the thioderivatives cause increased irritability of the cardiac muscle itself. In dogs the average cardiac rate increases from 82 to 210 beats per minute. Electrocardiographic studies also show alternate ventricular premature contractions (see Fig. 4) and occasionally periods of paroxysmal ventricular tachycardia. Such cardiac irregularities occurred in all of the experiments performed on dogs, cats, and rabbits. In monkeys, these changes were noted only following a previous injection of 5 mg. per kg. of morphine sulphate. Morphine sulphate seems to increase the toxic effects of the thiobarbiturates.

The rate of conduction of impulses over the bundle of His is also increased. In dogs the normal P-R interval is about  $\frac{3}{25}$  second. Following the injection of pentothal and other thioderivatives this time is decreased to about  $\frac{2}{25}$  second (Fig. 4). An occasional premature ventricular contraction was observed in one of the dogs after three injections of evipal, but the above irregularity was never observed with the other barbiturates. Inasmuch as these cardiac findings were never recorded with the use of sodium pentobarbital, we must assume that the change in cardiac activity must be due to the sulphur in the thiobarbiturate. The thioderivatives appear to be, therefore, more dangerous than the ordinary barbiturates.

The third source of danger is that the rapid injection of any of the barbiturates causes a sudden fall in blood pressure (see Figs. 1 and 2). This fall is mainly due to cardiac injury and dilatation of the arterioles, capillaries, and venules of all the organs of the body.<sup>17</sup> Evipal and the thioderivatives are less prone to cause marked falls in blood pressure in dogs, especially on repeated injections. This difference no doubt is due to the increased volume output by the organ as a result of the cardiac acceleration. With the thioderivatives some of our animals showed an increase in cardiac rate of over 150 beats per minute with a concomitant increase in blood pressure.

The change in the vascular bed is also reflected in the lungs. Acute edema of the lungs may result and upon the recovery of the animal bronchopneumonia<sup>28</sup> may occur. In human beings as little as 3 gr. of nembutal may produce this effect. Skin rashes and changes in the mucous membranes of the mouth may also be noted, with toxic doses, or



with therapeutic doses in individuals who are hypersensitive to these drugs. Leucocytosis was recorded by Warner<sup>29</sup> following sodium amylal injection in rats.

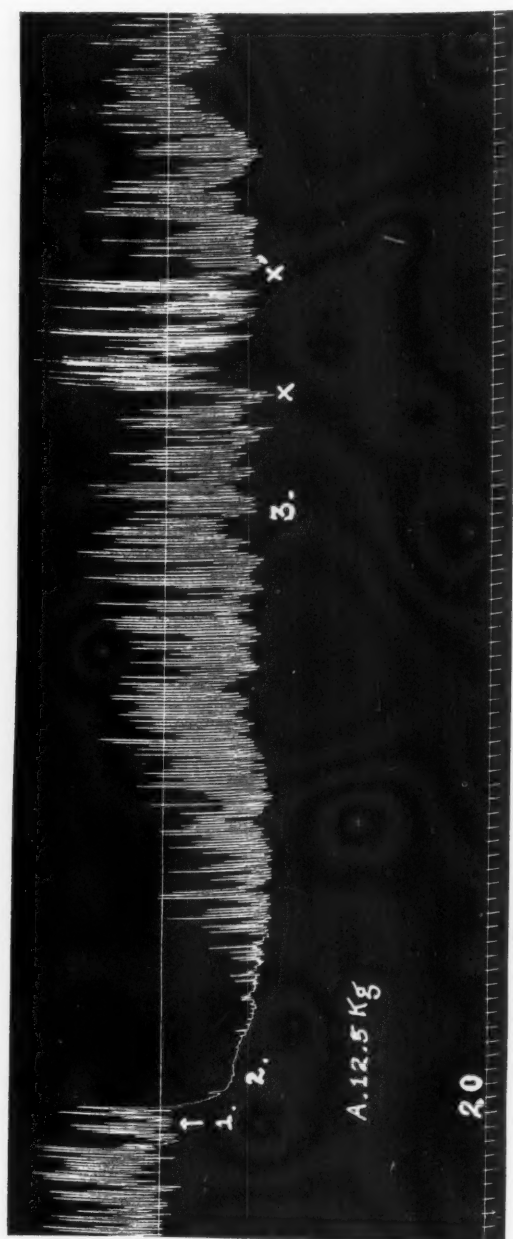


Fig. 5.—Dog weighing 12.5 kg. with Thirty-Vella loop of the jejunum. Balloon method used in recording the contractions and the changes in general tonus of the gut. The balloon measured 20 mm. in diameter and 50 mm. in length. The internal pressure was 15 cm. of water. Top record, the muscular contractions of the gut and the bottom record, the time in intervals of twenty seconds. Between 1 and 2, 300 mg. of sodium amylal were injected intravenously. Disappearance of rhythmic contractions as well as decreased general tonus can be noted. At 3 the animal woke up and at x and again at x' the animal became very excited.

The changes in the blood pressure in human subjects are very variable. All authors who have used these drugs in obstetrics report some increases and some decreases in blood pressure. Apparently the extreme drop does

not exceed 30 mm. of mercury.<sup>30</sup> However, it should be borne in mind that Galloway and Smith<sup>12</sup> report two cases of shock in their series.

The fourth source of danger lies in their depressant action on all smooth muscles, especially when large doses are given. We were able to study the effects of intravenous injection of these drugs in nonanesthetized dogs with Thiry-Vella loops of intestine.<sup>31</sup> In these animals invariably the ileum, jejunum, and duodenum relaxed following the intravenous injection of doses less than the anesthetic dose of the sodium barbiturates. Not only did the general tonus of the gut decrease but also the peristaltic contractions immediately ceased and the spontaneous

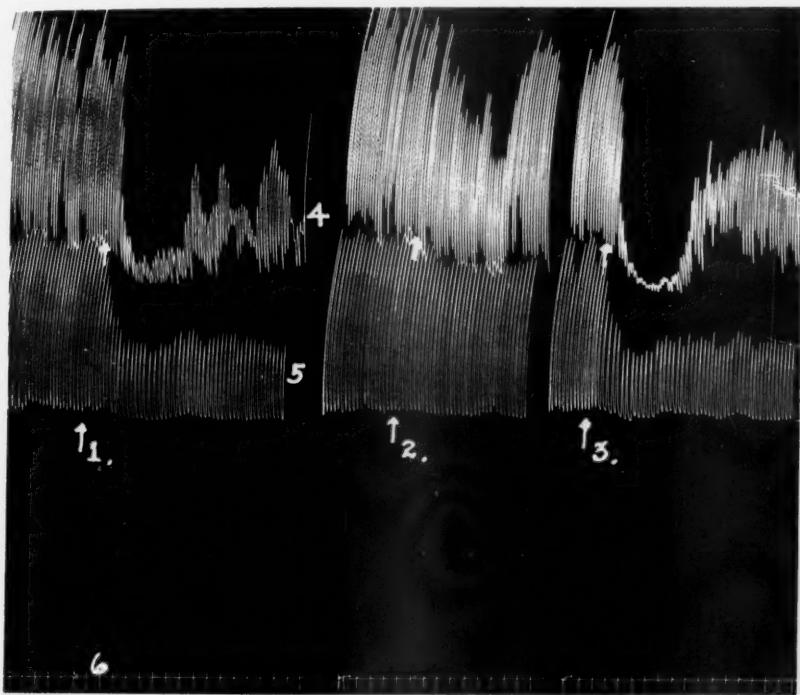


Fig. 6.—Excised longitudinal segments of rabbit intestine bathed in Tyrode-Locke's solution (equal parts) having a pH of 7.6. The solution was kept warm, 38° C. and oxygenated by bubbling air through it. The time is in intervals of twenty seconds. 4, Duodenal segment. 5, Ileal segment. 1 and 3, the effect of ortal sodium, 1:25000 solution with a pH 8.2. 2, Effect of amytal sodium, 1:25000 solution with a pH 8.6.

rhythmic contractions diminished in force and ultimately disappeared completely (see Fig. 5). We also studied the effects of these drugs on excised segments of rabbit and cat intestine bathed with warm oxygenated Tyrode's solution<sup>32</sup> (see Fig. 6). In all cases if the pH of the bath is controlled, the true barbiturates when added to the bath invariably cause decreased tonus and with it a decrease in the force of the rhythmic contractions. A comparison of the results in Fig. 6 would seem to indicate that ortal sodium is more depressant than sodium

amytal. This is true only in excised segments. In the living animal, sodium amytal produces not only a greater decrease in the general tonus, but also a more prolonged decrease in both the force of the contractions and general tonus. The thiobarbiturates, especially pentothal and thio-



Fig. 7.—Longitudinal segments of excised rabbit uterus immersed in Locke's solution. The solution had a pH of 7.6, was kept at 38° C. and was oxygenated by bubbling oxygen through it. At 1, sodium amytal was added to the solution, making a 1:5000 dilution. At 2, the amytal solution was drained and replaced by fresh Locke's solution. As a result of the drug marked loss of tonus and disappearance of the rhythmic contractions can be seen.

pentobarbital, cause a temporary increase in tonus and with high concentrations this is followed by marked loss of tonus and complete disappearance of the rhythmical contractions. From these findings it would appear that postdelivery gas pains may not only be accentuated when present but they may even be initiated by these drugs. Loss of general tonus is also noted in the ureter and urinary bladder. This no doubt would necessitate more frequent catheterization in women following

delivery. I was unable to find statistics to support either inference upon critical analysis of the clinical reports.

The effects of these drugs upon the human uterus appear to be variable. Some writers claim no delay in delivery others report complete cessation of the contractions of the uterus for two hours.<sup>21</sup> The intact and excised guinea pig uteri were studied by Drabkin and others.<sup>33</sup> Amytal anesthesia, they claim, does not abolish the rhythmical contractions nor does it decrease the oxytocic action of pituitary extract. In most of our experiments, we used excised segments of cat and rabbit uteri in a bath of warm oxygenated Locke's solution. The addition of any of the barbiturates or thiobarbiturates to it caused immediate loss of general tonus and decreased rhythmical contractions (Fig. 7). This depressant action varied with the different barbiturates. Generally speaking, the degree and duration of action were greater with the longer acting than with the shorter acting barbiturates. Thus, it was found in order to produce the same degree of depression a much more concentrated solution was needed of sodium evipal than of sodium pentobarbital, etc. We noted marked reduction in tonus of the intact uterus and vagina in dogs anesthetized with these drugs. Morehead and Mussy<sup>34</sup> report marked relaxation of the cervix and perineal muscles following the oral use of sodium amytal in human beings. Their findings have been confirmed by Ruth and Paxson.<sup>9</sup> Bohler,<sup>10</sup> using pernocton, reports 10 cases in which a decrease in uterine contraction existed following the expulsion of the fetus and placenta. A slowed contraction of the uterus in 4 per cent of his cases was reported by Boylan<sup>13</sup> with the use of sodium pentobarbital. Levy-Solal and Sureau<sup>21</sup> have shown with the use of evipal that the decreased tonus and contraction of the human uterus is directly proportional to the depth of anesthesia. In 6 of their 46 cases under profound narcosis, the forceps had to be used. They also point out the fact that the second injection of evipal caused greater depression of the uterus than did the first. This is in keeping with our findings on the anesthetic action of this drug. The duration of anesthesia is increased with each injection of the anesthetic dose in dogs. These findings, we believe, might be one of the causes for the frequent need to use the obstetric forceps in the delivery of these patients. Some obstetricians, according to their writings, used the obstetric forceps in about one-half of their cases. Galloway and Smith,<sup>12</sup> using nembutal and scopolamine, report only 4 spontaneous deliveries in 275 primiparous and 119 spontaneous deliveries in 227 multiparous cases. They also report increased bleeding in 20 cases. Averett,<sup>22</sup> using the same anesthetic agents, reports 25 spontaneous deliveries and the use of the forceps in 131 cases in his series. Le Lorier and Mayer<sup>35</sup> noted severe hemorrhages after delivery in 3 of the 26 patients in whom evipan was employed.

There appears to be no delay in the delivery of the child with the use of these anesthetic agents. It may be that the restlessness and the spontaneous contractions of the striated muscles of the abdomen may hasten the complete dilatation of the cervix and soft parts of the birth canal which are already in a relaxed state due to the action of the drug.

#### CONCLUSIONS

In selected cases, and if given properly, the barbiturates may be fairly safe. In the hands of many, if they are used as anesthetics in unselected cases, they will be found to be dangerous drugs both to the mother and

to the unborn fetus. I feel that they should be given either by a competent anesthetist or used only as hypnotic drugs.

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## DISCUSSION

DR. HENRY S. RUTH.—I am under the impression that the gradation of psychic response and the reaction to pain is a most difficult one to evaluate by animal experimentation. Gruber's findings of cardiac irregularities developing with pentothal sodium I am sure are quite interesting to all of us who have been administering this drug and have found it quite satisfactory for a few various situations. I would like to ask Gruber if he has observed any likelihood that this response is possibly a reaction confined to the class of animals with which he has worked, in view of the fact that such irregularities have not, to my knowledge, been reported in the literature as having occurred in human beings. Lundy has reported 2,440 administrations in a twenty-month interval ending June of this year and makes no mention of such irregularities. I have been employing it somewhat during the past year and have observed a slight acceleration of the pulse rate but no arrhythmias. The fact that urologists at one large institution favor this anes-



thetic above all other anesthetic agents and methods for their endoscopic trans-urethral resections, which, of course, are usually indicated in old men, speaks for the possibility that their action on the cardiovascular system is a rather insignificant one.

It does not seem probable that these *shortest* acting barbiturates (evipal and pentothal sodium) with their analgesic properties will play a major part in the pain control in normal obstetrics, for in these affairs we desire and require longer action. We, therefore, should perhaps be more in order in this discussion by confining our remarks to the *shorter* acting barbiturates of the class of sodium amytal, pentobarbital sodium, etc. Their pharmacologic action is similar when considered as a class. They are depressing to metabolism. It should be remembered that they are essentially soporifics, acting primarily on the intellectual centers, and have but very slight analgesic action. When sufficient dosage has been prescribed to prevent pain perception, the vital reflexes are dangerously depressed. The amounts required of them to produce a given therapeutic effect in their clinical application bear approximately the same relationship to the minimum lethal dose; for example, pentobarbital sodium is twice as toxic as sodium amytal but only one-half as much is required to produce comparative effects. When too large dosages incur complications, the shorter acting barbiturates are fatal through respiratory depression and the longer acting ones through pulmonary complications, edema, and pneumonia. Idiosyncrasies are perhaps no more common than occur with morphine and should be combated by oxygen therapy, and coramine intravenously or intramuscularly, metrazol subcutaneously or intravenously, or perhaps by picrotoxin. Whereas it is true that these drugs depress the involuntary musculature, it has been shown by many investigators that the resistance of the uterine muscle fibers in situ is quite high.

I believe that a little plan employed by many of us to determine the dosage of preanesthetic sedatives might prove of value to select the dosage of the barbiturates for various individuals. By this plan we take cognizance of the fact that to obtain beneficial effective preanesthetic sedation several factors must be considered.

It has been shown, especially by Guedel, that the curve of reflex nerve irritability parallels the curve of metabolism; cell oxygen demands, of course, parallel metabolism. The amount of an anesthetic agent to provide a given depth of anesthesia will increase or decrease in a direct ratio with an increase or decrease of metabolism. Therefore, a curve over the required amount of anesthesia parallels closely the curve of metabolism. We desire normal metabolism in order to decrease the amount of anesthesia. Therefore, an estimation of the factors which cause a deviation in the basal metabolic rate will yield indispensable evidence which will serve as an aid for the correct dosage for each individual.

One of the most important factors, because of its consistent application, is the effect of age upon the metabolic curve; but because this is of small relative importance in obstetrics, the normal metabolic curve for various ages will merely be drawn upon the blackboard without further elaboration. Another factor is that of temperature; for each degree of fever there is a 7 per cent increase in metabolism. Emotional activity, such as fear, apprehension and anger will exert a profound influence usually in the upward direction, but this can only be estimated and not measured. Pain exerts a substantial effect in direct ratio to its severity. Specific toxemias, of which thyrotoxicosis and neurosyphilis are notable, raise reflex nerve irritability and therefore resistance to hypnotic sedation. Drug addicts and alcoholics also show a resistance. The body weight of the individual is of some importance when the excess weight is not due to fat; the factor of sthenicity is of greater importance. We shall illustrate on this metabolic curve on the board the effect of some of these factors, and how they will influence the dosage of the

class of drugs under consideration. If immediately below this curve of metabolism we draw the four stages of anesthesia, the practical application will become more apparent. The first stage of anesthesia is the stage of analgesia, the upper portion of which consists of relative analgesia which increases in intensity as the lower border of the stage is reached, until at the very lowest border a narrow margin of total analgesia is obtained just before entering the second stage. The second stage is the stage of delirium. Below this, of course, appears the third or surgical stage with its four strata and finally, the fourth stage. With both of these latter two, however, we are not concerned at this time.

By the use of drugs producing analgesia we can enter the first stage, and, if we are fortunate, place the patient in total analgesia. I should like to repeat, however, that the barbiturates are essentially hypnotic and are but mildly analgesic. When the dosage is increased beyond certain limits in an effort to reach total analgesia, the patient will be thrown into the stage of delirium, and restlessness results. Because the barbiturates are more amnesic than analgesic in action, it is better to be satisfied with a loss of memory of the pain alone by their use, for we will repeat, when sufficient dosage has been prescribed to prevent pain perception, the vital reflexes are dangerously depressed. If, in a situation of such depression an inhalation anesthetic is superimposed, in order to keep the patient quiet for the actual delivery, a fatality may easily be encountered if the anesthetist is not aware of both the presence and the dangers of this depression.

DR. J. O. ARNOLD.—We have failed to be convinced, through the years since the barbiturates have been in vogue, that their use could be as successfully or as satisfactorily practiced in the homes as in the hospitals. Therefore, after trying out one after another of these newer combinations, we have practically dropped them all, and gone back to older, more reliable and less troublesome methods. Many years before the outbreak of the "twilight sleep" epidemic we had been using morphia and scopolamine, and when that procedure had been pushed to the extreme by the popular press, we swung over to the morphia and magnesium sulphate combination, after the technic of Gwathmey. Then came the barbiturates, but now for about three years we have given these up also, and gone back once more to a modified Gwathmey course, dropping the magnesium sulphate, and giving the plain morphia, followed more or less closely by "E.O.Q."—ether, oil, and quinine, by bowel. We are convinced that our present results are as good as with any other method we have pursued, and much less complicated and troublesome to apply.

The effects on the mothers, mentally and physically, are certainly no less satisfactory than those produced by the barbiturates. The supervising maternity nurse, who has been on the service for many years and has observed all these varying procedures in the hands of many different doctors, is unqualified in her endorsement of our present methods. A review of our records for the past three years shows also a steadily lowering infant mortality, which would hardly be the case if we had many narcotized babies.

I am quite sure that if we follow these old-fashioned methods with as much attention and care in their clinical application as is being devoted to the safeguarding of the barbiturate victims, we shall get better all-around results. Furthermore, we will have something to teach our students that will not only be safer, but that will undoubtedly be more generally applicable under the conditions in which most of their work will be done, where special nurses and sideboarded beds, and all that sort of expensive equipment can seldom be provided.

DR. PHILIP WILLIAMS.—During the past few years those of us who have attended the monthly reviews on Maternal Mortality at the Philadelphia County Medical Society realize that there have been a number of cases, possibly 18 or 20,

in which the administration of the barbiturates during the labor has had a certain degree of influence toward the fatal outcome of these cases.

In some instances, no other factors could be elicited and the death was undoubtedly due to some action of the sedative. In others, the depression caused by the drug placed the patient in jeopardy when inhalation anesthesia and operative procedures of various types were added to the burden already carried. In the remaining cases, the drugs used may or may not have played a part in the death.

As has been expressed many times the most important requirement of a sedative agent lies in the safety of its use. We cannot grant that the barbiturates are perfectly safe to use in all labors. The idiosyncrasy of the patient to the drug must be taken into account. In not less than three cases, an idiosyncrasy was manifested by the development of cyanosis, respiratory embarrassment, and edema of the lungs with increasing shock from which the patients did not recover.

The susceptibility of a patient to the barbiturates or a patient's tolerance to the barbiturates form questions as yet unsolved. The prolonged coma in which some parturient women remain after the average or ordinary dose of such sedation proves without doubt that occasionally some individuals possess a high susceptibility to the action of these agents, while others are unusually tolerant and may require much more than the average dose before sedation is produced. In a number of the patients where labor had ceased with the patient in the peculiar deep coma following exhibition of barbiturates, ether anesthesia and major procedures were followed at times by uncontrollable postpartum hemorrhage, at other times by shock and collapse which resisted the usual measures of treatment.

In the remaining cases, while the barbiturates may or may not have played a part in the fatal outcome, it was evident to those who heard the discussion of such cases that the barbituric acid derivatives formed a dangerous background to an operative delivery.

I feel that the element of safety in the use of these drugs has not been entirely proved, and a considerable degree of caution, especially as to the dosage, must be exercised before they are exhibited in the patient who may require major obstetric procedure for delivery.

DR. CLIFFORD B. LULL.—I cannot agree with the things that have been said, as the use of this group of drugs in the practice of obstetrics has slowly but surely raised my enthusiasm for them. The important thing to remember is when and how to use these drugs in obstetric work, and I believe that if nembutal and scopolamine are used properly, the danger arising will be minimized.

In experience extending over approximately three and a half years, and in about 4,000 cases, I have not seen the serious complications that I have seen without the use of analgesia, or with the use of other analgesic remedies. As far as increasing my operative percentage of deliveries, it has not done so, because my operative deliveries in private cases have been almost 100 per cent. I believe the mistake is being made by classifying outlet forceps, that is, when the head is crowning, as an operative procedure. I admit, with the use of these drugs, that this is usually essential because the patients are restless with the pains, and if they are not delivered under light nitrous oxide anesthesia, the operative field might be contaminated. I am convinced, however, that by the use of these drugs, the more difficult forceps operations and the incidence of version have been very decidedly decreased. I have not seen postpartum hemorrhage, neither have I seen narcotized children. Further, I am convinced that the duration of labor, particularly in nulliparous individuals, is decidedly shortened, and I am certain that the cervical traumatism has been very markedly decreased.

When I first started to use nembutal and scopolamine, I used it in a dosage of 4.5 gr.; but for the last eight or nine months I have been giving almost routinely 9 gr. nembutal and 1/150 scopolamine as an initial dose, and giving it as early as possible. In other words, as soon as I was certain that the patient was in labor, irrespective of the amount of dilatation or effacement. Giving these drugs early in labor unquestionably gave better results. The amount of excitation in the individual patient has been markedly decreased by giving a larger dose of the drug, and we have also found that in the occasional patients who become wildly excited, the addition of rectal ether will quiet them down, particularly if the rectal ether is given while the patient is under light nitrous oxide anesthesia.

In conclusion, I realize that we are dealing here with drugs that, if used promiscuously and in private homes or in poorly equipped institutions, might increase the dangers to both mother and child, but I feel very strongly that any woman, no matter from what stratum of society, is entitled to the relief of the pains of childbirth, if it can be done with safety to both her and her unborn child. Until some different method is evolved, or until I see some of the dangers which are now attributed to these drugs, I shall continue to endorse their use and continue to use them.

DR. EDWARD SCHUMANN.—I wish to call your attention to three or four points.

The first is that only within the last few years have women demanded amnesia in labor. From the time of Simpson and before, relief of pain was sought. Now this has suddenly become secondary, and it is of exceeding importance that the woman does not remember that she has been in labor. That has been bolstered, mainly, by current literature and lay magazines.

The second point is, and I think all of us will agree, that the more profound the analgesia the greater the inhibition of normal mechanism of labor, and therefore since it is in the minds of some of us to return to a greater degree of normalcy in the conduct of obstetrics and to secure, if possible, the highest percentage of spontaneous deliveries, we must lessen the degree of analgesia which we present to our patients.

The third point is the fact that we have got to a point, where we are controlled by our patients with regard to analgesia, and I consider this grave from the standpoint of the medical profession. The patient demands painless labor. I believe, as a group we should confront the patient with the statement that we choose the analgesia and conduct the labor to her best interests.

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**Banerji, Kaligati: A Study of Maternal Mortality and Morbidity in Bengal, J. Indian M. A. 5: 607, 1936.**

The author deplors the prevailing poor conditions in Bengal. The maternal mortality rate is high. Per 1,000 births in India, there is a mortality of 16.6 in Madras City and of 42 in Tea Gardens in Assam.

Bengal requires a well-planned organization and a good scheme of cooperation to institute proper maternal care, both prenatally and intrapartum. The midwives (dais), as they exist at present, are inefficient, untrained, incapable and a source of sepsis to the parturient.

The hospital should have an antenatal clinic under a trained doctor and midwives. The mothers need to be advised as to proper food and living during pregnancy, labor, and the puerperium. They must be taught to report to the thana clinic if abnormalities occur. A strict program of public health must be initiated if the gross mortality and morbidity are to be reduced.

F. L. ADAIR AND S. A. PEARL.

## ANALGESIA WITH THE BARBITURIC ACID DERIVATIVES AND ITS RELATIONSHIP TO SUDDEN DEATH IN LABOR\*

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NO TOPIC in obstetric procedure is more provocative of discussion than that of analgesia and anesthesia. Journals are filled with reports of assorted methods and new combinations, and every patient who comes to register wants first to know what will be done to eliminate the pangs of labor. She wishes to go to sleep with the first pain and wake with the baby in her arms, and she is sure from her reading that this is not only feasible but it is her rightful privilege.

Particularly has this been true since the introduction of the barbituric acid derivatives. Immature intimations as to the success of these products have been avidly seized upon by the public. Certain women's magazines make of each new obstetric analgesia their protégé, announce it as the panacea for women's suffering and the remedy without which any physician who assays to practice medicine is a nonentity or a Rip Van Winkle. Thus the manner of sensationalizing which started thirty years ago in the far-flung propaganda for "twilight sleep," and which repeated itself in the case of Gwathmey anesthesia and pernocton, is now busied with the newer forms, amytal and nembutal.

Just as occurred with each of the previous methods, the time comes to weigh carefully in the balance the safety and the therapeutic effectiveness of these agents.

From various sources, doubt has arisen as to the effect which deep analgesia and anesthesia have upon the intelligent and safe conduct of labor. In its much criticized report on "Maternal Mortality in New York City," the Committee on Public Health Relations of the New York Academy of Medicine state the following in reference to this question:

"The use of anesthesia during labor and delivery has grown steadily in extent since its introduction in the last century, and is a problem of the most pressing importance, more so in the United States than in any country. This has come about to a large extent through pressure from the lay public. The women of the large urban centers have become steadily more insistent in their demands for shorter and less painful parturition, and the accoucheur may disregard these demands only at great risk to his own practice."

\*Presented at a meeting of the Obstetrical Society of Philadelphia, November 5, 1936.



The committee is of the opinion that "frequent and injudicious employment of deep analgesia and anesthesia has increased very materially the rate of operative interference, and has on this account been a major factor in preventing a reduction in the high maternal mortality rate in this country."

Before condemning these assertions as reactionary, let us turn to the results of maternal welfare study in Philadelphia and ascertain how we are progressing with the management of labor and how our results are influenced by deep obstetric analgesia and anesthesia.

While the general maternal mortality rate in Philadelphia has decreased 24 per cent from 1931 to 1935, this decrease is accounted for solely on the basis of a 49 per cent decline in nonpreventable deaths. The preventable death rate has remained uniform throughout the five years. While the death rate per 10,000 live-births, which is attributable to errors in judgment and technic on the part of the physician, has decreased 9.5 per cent, yet the proportion of maternal deaths due to these errors has increased 11 per cent.

If one considers the maternal deaths during or within twenty-four hours after labor, the rate of preventable deaths and the share in responsibility of the physician for them rises amazingly. In this group there is no change in the maternal death rate for the five-year period. The nonpreventable death rate has decreased 49.3 per cent; the preventable rate has risen 52.5 per cent. The death rate from errors in judgment and technic on the part of the physician as manifested in sudden deaths at delivery has jumped 108.5 per cent, and the proportion of maternal deaths due to these errors has increased 107.3 per cent.

When these statistics are assembled, one may conclude that here is the explanation of our failure to progress. A consideration of the death rate from all other conditions of childbearing confirms this opinion. In this group there is a decrease in the maternal death rate of 28.9 per cent, in the nonpreventable death rate of 48.6 per cent, in the preventable rate of 11.1 per cent, in the death rate from errors of judgment and of technic on the part of the physician of 41.4 per cent, and in the proportion of deaths due to these errors of 5.5 per cent.

A general reduction of mortality in all its phases then in 876 of 1,096 cases, but no reduction in mortality in the remaining 220! An improvement in all phases of obstetric practice except those which have to do with labor, and in the latter an increase of over 100 per cent in the responsibility of the physician for sudden death! End-result, no change for five years in the preventable maternal death rate; instead, a general increase of 11.1 per cent in the proportion of maternal deaths due to errors in judgment and technic on the part of the physician!

Evidently something is wrong with our methods of management in labor, and saddest to relate, whatever is wrong is going "more wrong" in every succeeding year.

Probably there are a number of points that are amiss in the conduct of labor, and doubtless it is a mistake to attribute these disturbing trends to faults in obstetric analgesia and anesthesia. Nevertheless, when one analyzes the methods used in the fatal cases and the part that the methods played in fatality, this consideration assumes a major importance.

The records reveal that in six of eleven instances in which nembutal was used, death was attributable to the analgesia, quite evidently in two, quite probably in the other four. In two additional instances the choice of the analgesic method, in view of the patients' condition, seemed singularly bad. In the eight instances of amytal administration there were two in which the analgesia was quite possibly the cause of death and two in which the selection of the method seemed injudicious.

While it is most difficult to say certainly that the analgesic method was responsible for the fatality, yet the evidence is preponderantly in that direction. The suspected cases had these points in common: there was no other factor of enough significance to account for fatality; all the patients succumbed with a peculiar type of cyanosis and respiratory depression, rapid thready pulse, and shock without hemorrhage which failed to react to the usual methods of treatment. In several instances the deaths were ascribed to heart failure or to pulmonary embolism. If this were the true diagnosis, it is peculiar that so many instances should have occurred in the barbituric acid group. Of the frequently made diagnosis "pulmonary embolism" Kerr says: "There is little doubt that a considerable number of deaths are attributed to pulmonary embolism which should really be relegated to trauma or shock or both. The diagnosis of embolus is a simple explanation and salves the conscience of the person in attendance."

The barbiturates are presumed to have a fairly wide margin of therapeutic safety. This is said to be the case particularly of sodium pentobarbital, or nembutal (Sollman). The reports of Irving,<sup>8</sup> Galloway,<sup>5</sup> and Daichman<sup>4</sup> reveal no maternal anesthetic death. There seems, however, to be a wide range of susceptibility to the action of the drug. For instance Galloway describes one case in which 22 gr. of nembutal were administered in the course of labor without any apparent effect, and the patient at the conclusion stated that she thought she had had a very hard time. On the other hand, Willcox, in the *British Medical Journal* of 1934 (1:417-418), emphasizes the importance of peculiar susceptibility to the drug and states that he has seen a number of cases in which sudden collapse, respiratory depression, and death from bronchopneumonia occurred, where only 3 gr. were administered. He particularly opposes the use of the drug as a preparatory or basal anesthetic.

For their effectiveness in labor the barbiturates depend upon ability to produce forgetfulness (amnesia) and very little upon analgesia.

Their action in the former direction is greatly enhanced by the addition of scopolamine. The patient may scream as if in great agony during the course of her labor pains, but wake the morning after with no clear recollection of what has taken place. In his analysis of obstetric analgesias, Irving states that he considers no method successful which gives less than 100 per cent amnesia. The factor of relief from pain he considers a minor consideration.

The advocates of the method claim that their drug supplants morphine, having none of its disadvantages and many advantages. They state that it does not delay labor, does not narcotize the baby, and that it makes the patient forget the unpleasant experience of childbearing. Several maintain that morphine has no further place in obstetric practice because of its ill effect on fetal respiration.

A great disadvantage of the barbiturates is the restlessness they produce. Patients under their influence may prove difficult to control. In such a confused and semistuporous state of mind, pain arising from the uterine contraction is misinterpreted, and the parturient becomes uncontrollable. As the time for actual delivery approaches, the confusion increases. Careful surgical preparation and spontaneous delivery under such circumstances are impossible. Usually the patient must be anesthetized with gas or ether and delivery consummated by low or mid-forceps. The labor over and the pains dispatched, the patient falls into a deep slumber and remains almost comatose for a number of hours.

The most enthusiastic users of the nembutal scopolamine technic acknowledge that the rate of operative interference is thereby multiplied many times, that forceps delivery becomes essential in from 40 to 60 per cent of cases. They also emphasize that patients under the influence of nembutal must be watched with the closest attention, their care individualized, and precautions taken that no injuries occur during the

TABLE I. HOW IS THE MEDICAL PROFESSION FULFILLING ITS RESPONSIBILITIES IN THE VARIOUS GROUPS OF MATERNAL DEATHS? 1931 VS. 1935

	ALL MATERNAL DEATHS	MATERNAL DEATHS DURING OR 24 HR. AFTER DELIVERY	ALL OTHER MATERNAL DEATHS
Maternal death rate	Decrease of 24%	No change	Decrease of 28.9%
Nonpreventable death rate	Decrease of 48.9%	Decrease of 49.3%	Decrease of 48.6%
Preventable death rate	No change (1%)	Increase of 52%	Decrease of 11.1%
Death rate from errors in judgment and technic on part of physician	Decrease of 9.5%	Increase of 108.5%	Decrease of 41.4%
Proportion of deaths due to errors in judgment and technic on part of physi- cian	Increase of 11.1%	Increase of 107.3%	Decrease of 5.5%

more restless periods. For this reason the method is available for use only in the hospital; it can only be a source of grief if undertaken in the home.

TABLE II. AMNESICS, ANALGESICS, AND ANESTHETICS EMPLOYED IN THE PATIENTS WHO DIED DURING OR WITHIN 24 HOURS AFTER LABOR

AGENT USED	NUMBER OF DEATHS IN WHICH AGENT WAS EMPLOYED	PRIMARY CAUSE OF DEATH	POSSIBLE CAUSE OF DEATH	POORLY SELECTED
Ether or nitrous oxide, oxygen, ether	108	1 (1%)	1 (1%)	1 (1%)
Nitrous oxide, oxygen	34	0	1 (3%)	9 (26%)
Gwathmey	7	0	3 (43%)	1 (14%)
Chloroform	3	0	1 (33%)	2 (66%)
Spinal	4	2 (50%)	1 (25%)	1 (25%)
Local	4	0	0	0
Nembutal	11*	2 (18%)	4 (36%)	2 (18%)
Amytal	8*	0	2 (25%)	2 (25%)
None	40	0	0	0

\*Possibly more. These deaths are being subjected to further study.

Considering these facts, one questions whether nembutal-scopolamine amnesia fulfills the requirement of safety. If the patient is in constant danger of injuring or contaminating herself, if her cooperation in the course of labor is utterly lost, if the incidence of operative interference is multiplied tenfold, if the supervision of the case is transformed from an intelligent conduct of labor into the treatment of drug confusion, one doubts that the effect is worth the reaction that it produces.

This method is at the height of its popularity. Reports of recent publication have been favorable, as they are always at such time. However, now that the method is getting away from the centers of its propagation and is being put into more general use, questions are arising as to efficacy, difficulty of management, and sudden death. In the crucible of general usage, the gold is separating from the sludge and that which is materially and permanently worth while is being refined.

In the light of such relentless scrutiny, it appears uncertain that deep analgesia with the barbiturates is completely safe or fully reliable. It is questionable whether the widespread acceptance of this method is a step forward in obstetric practice.

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1930 CHESTNUT STREET

### EFFECTS UPON UTERINE MOTILITY OF URINE FROM DYSMENORRHEIC AND NORMAL INDIVIDUALS\*

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THE present investigation was undertaken in an effort to gain some information concerning the factors underlying essential dysmenorrhea. In spite of the importance of this disorder, comparatively little experimental work on its cause and essential features has been done. The nature of menstrual pain has led clinicians to attribute it to spasmodic or exaggerated contraction of the uterus, an assumption which is supported by the fact that the spontaneous motility and the sensitivity of the human uterus are especially marked just before and during menstruation.<sup>1</sup> Moir,<sup>2</sup> using an intrauterine bag, obtained records of uterine contractions and intrauterine pressure in a patient with dysmenorrhea and in a normally menstruating woman. The chief point of difference was in the pressure, which reached a maximum of 150 mm. of mercury in the dysmenorrheic patient, as compared with 120 mm. in the normal woman.

To explain the underlying cause of the painful contractions, a number of theories have been advanced. They have recently been reviewed by Novak and Reynolds<sup>3</sup> and by Israel.<sup>4</sup> Those of widest application postulate abnormal variations in humoral factors influencing uterine motility. An examination of the action of blood or urine upon uterine motility seemed, therefore, a logical method of approach to the study of dysmenorrhea, especially since results reported by a number of investigators indicate that certain variations in the effects of blood or urine obtained under different physiologic and pathologic conditions can be demonstrated.<sup>5-14</sup> Because it is readily obtainable in adequate quantities, urine was chosen for investigation in the present study. This includes a series of experiments in which tests were made of the action

\*The data in this paper are taken from a thesis presented to the Graduate School of Vanderbilt University in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Anatomy. The work was done under the supervision of Dr. J. M. Wolfe, Assistant Professor of Anatomy. The experimental methods and data, which have been presented in greatly abbreviated form, will be published in full in the author's thesis, which is available in the Vanderbilt University Library.



upon uterine motility of urine obtained from women who experienced varying degrees of menstrual discomfort. Urine from men was used as controls.

#### METHODS

Degrees of menstrual discomfort were defined as follows: *Dysmenorrhea*, menstrual cramps of incapacitating severity. *Mild cramps*, menstrual cramps of minor severity which interfere in no way with usual activities and which are relieved by mild medication. *No cramps*, a condition in which menstruation is accompanied by no cramps, although there may be a minor degree of vague general discomfort.

Urine was obtained from 37 individuals: 10 women with dysmenorrhea, 12 women with variable menstrual symptoms, 7 women with no cramps, and 8 men. In all of the cases of dysmenorrhea, pelvic pathology as an etiologic factor could be excluded.\*

Single urine specimens were obtained from men. Specimens from women were collected, as a rule, during two or more consecutive menstrual periods and at intervals of one week or less during the intermenstruum. Intermenstrual specimens were classified according to the degree of discomfort present at the following menstrual period. One hundred and seventy-three specimens of urine were investigated. Their distribution with respect to sex, to phases of the menstrual cycle, and to the degree of menstrual discomfort is shown in Table I.

By means of the uterine fistula technic developed by Reynolds,<sup>15</sup> the urine was tested for its effect upon the motility of the uterus in situ in unanesthetized, castrate rabbits. Uterine motility was recorded on a smoked drum by means of an intrauterine balloon connected to a tambour through a water and air transmitting system. Using this technic, Reynolds showed that after castration the uterus of the rabbit becomes quiescent<sup>16</sup> and does not respond to stimulation unless rhythmical motility has been induced by the administration of estrogen.<sup>16-18</sup> For this reason, the test animals were injected with estrogen† approximately twenty-four hours previous to the injection of urine.

In testing the urine, two procedures were followed. In the first, 0.2 c.c. of pituitrin‡ was injected thirty minutes after the injection of urine. The response to pituitrin served as a control of uterine sensitivity;<sup>19</sup> it was also useful in demonstrating certain effects of the urine. In the second procedure, which was adopted as an additional test of the effect of urine upon the response of the uterus to a subsequent injection of pituitrin, the pituitrin was injected one hour before and again ten to fifteen minutes after the injection of urine. Both urine and pituitrin were injected intravenously. The dosage of urine was not constant but was regulated by the response; this was necessary because of the toxicity of specimens voided during dysmenorrheic cramping. The maximum dose was 20 c.c. All urine specimens were tested as in Procedure 1§; 42 specimens from women, representing all of the groups shown in Table I, were also tested as in Procedure 2.

#### EXPERIMENTAL RESULTS

*Effects of Pituitrin.*—For purposes of comparison with effects obtained following the injection of urine, responses to pituitrin in animals not previously injected with urine (Procedure 2) are illustrated in Fig. 1. They were essentially similar

\*The suitability for the purposes of this study of the individuals from whom urine was obtained was approved by Dr. John C. Burch, Associate Professor of Obstetrics and Gynecology.

†Theelin, Parke, Davis and Company, or Progynon B, Schering Corporation.

‡Pituitrin-S, Parke, Davis and Company.

§In a few of the earlier experiments, pituitrin was omitted after positive responses to urine.

TABLE I. DISTRIBUTION OF TYPES OF RESPONSES AND OF POSITIVE OXYTOIC AND INHIBITORY EFFECTS, CONSIDERED SEPARATELY, IN RELATION TO THE CONDITIONS PRESENT AT THE TIME OF COLLECTION OF EACH SPECIMEN OF URINE

	PHASE OF MENSTRUAL CYCLE								MEN	TOTALS		
	DYSMENORRHEA				MILD CRAMPS						NO CRAMPS	
	MENSTRUATION SPECIMEN VOIDED DURING MOST SEVERE CRAMPS	MENSTRUATION SPECIMEN VOIDED BEFORE OR AFTER MOST SEVERE CRAMPS	INTER-MENSTRUUM	MENSTRUATION	INTER-MENSTRUUM	MENSTRUATION	INTER-MENSTRUUM	MENSTRUATION				
No. individuals represented	11	11	12	9	7	12	8	8	37*			
No. menstrual periods represented	14	14		15		19			58*			
No. menstrual cycles represented by intermenstrual specimens			15		12		11		38			
No. specimens investigated	15	19	36	20	30	20	25	8	173			
Responses in each group producing: Percent of all specimens in which:	Oxytocic phase positive; inhibitory phase positive	26.3	22.22	45.0	40.0	35.0	36.0	50.0				
	Oxytocic phase positive; inhibitory phase absent or insignificant	66.6	42.1	27.77	10.0	10.0	12.0	12.5				
	Oxytocic phase absent or insignificant; inhibitory phase positive	---	---	15.0	23.3	35.0	8.0					
	Insignificant responses	---	26.3	15.0	13.3	10.0	32.0	25.0				
	No demonstrable effect	---	5.3	15.0	13.3	10.0	12.0	12.5				
Positive oxytocic effects (considered separately)	100.0	68.4	50.00	55.0	50.0	45.0	48.0	62.5				
Positive inhibitory effects (considered separately)	33.3	26.3	50.0	60.0	63.3	70.0	44.0	50.0				

\*In some instances, the same individual or the same menstrual period is represented more than once. This is due to the fact that some women experienced different degrees of menstrual discomfort at different periods investigated and also to the fact that, in some instances, more than one urine specimen was collected at a single menstrual period.

to those described by Reynolds;<sup>19</sup> i.e., an initial oxytocic effect was followed by a period in which the rhythmical motility was inhibited to a greater or less extent. Evidence of both oxytocic and inhibitory effects was present in all of the records obtained; oxytocic effects were invariably strong, but inhibitory effects were slight in about 20 per cent of the tests (Fig. 1, C). Following the response to pituitrin, the return to motility of the original type and degree was gradual; it was usually complete one hour after the injection. Responses to urine injected at this time were often reduced in magnitude, which indicates that decreased sensitivity of the uterus due to pituitrin may persist after the return of rhythmical motility.

Responses of the uterus to pituitrin in animals previously injected with urine (Procedure 1) were in every way similar to those described above, except that they were sometimes reduced in magnitude. Occasionally the initial tetanus was incomplete (Fig. 3).

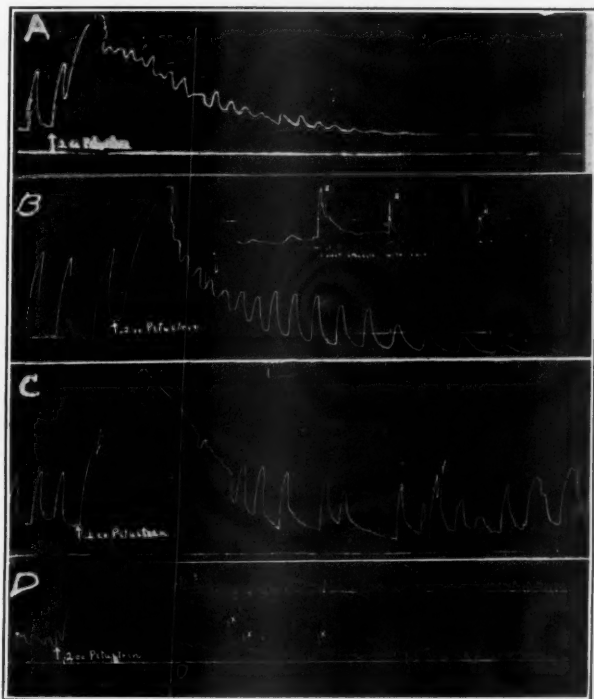


Fig. 1.—Uterine responses to pituitrin in animals not previously injected with urine. x, micturition.

*Effects of Urine.*—The basic response of the uterus to urine consisted of an initial phase of contraction (oxytocic phase) (Fig. 2), followed by a decrease in the degree of rhythmical motility and a reduction in the sensitivity of the uterus to pituitrin (inhibitory phase). In 60 responses, the inhibitory effect upon the rhythmical motility was indicated by a period of relative quiescence similar to that produced by pituitrin (Figs. 3 and 5). These responses were followed by gradual return of the original motility. In 28 responses, the inhibitory effect was indicated by a gradual decrease in the amplitude of the rhythmical contractions with no return to motility of the original degree (Fig. 6).

The responses produced by different specimens of urine varied in magnitude with respect to one or both phases. In 59 responses both oxytocic and inhibitory

phases were positive (Fig. 3). In 39 responses the oxytocic phase was positive, the inhibitory phase absent or insignificant in magnitude (Fig. 4). In 29 responses the oxytocic phase was absent or insignificant, the inhibitory phase positive

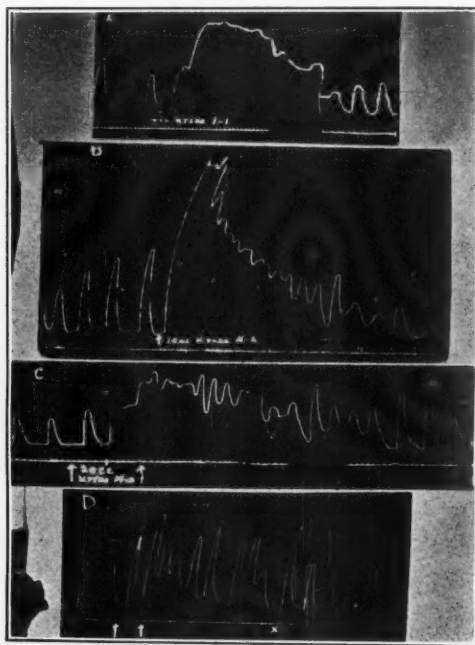


Fig. 2.—Responses to urine showing oxytocic effects. A, B, C, Positive oxytocic effects. D, Insignificant oxytocic effect.

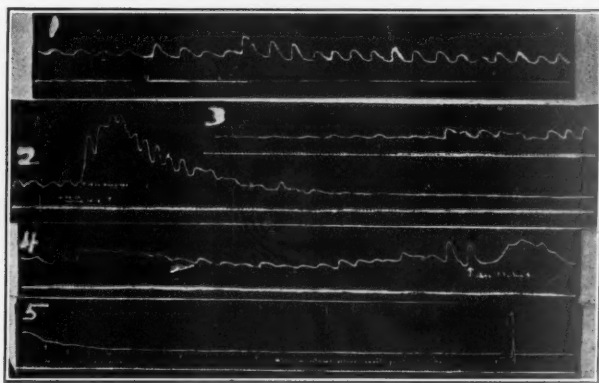


Fig. 3.—Response to urine (Tracing 2) in which both oxytocic and inhibitory phases were positive. Response to pituitrin (Tracing 4) reduced in magnitude (compare with Fig. 1, D).

(Figs. 5 and 6). In 30 responses one or both phases were present but insignificant (Fig. 2, D). Sixteen specimens of urine produced no demonstrable effect.

The responses obtained were related to the conditions present at the time of collection of each specimen of urine as shown in Table I and in Charts I and II. The table and charts also show the distribution of positive oxytocic and inhibitory effects considered separately.

The percentage of positive oxytocic effects was markedly greater, as compared with all other conditions, in association with dysmenorrhea (Chart I, complete graphs). Every specimen collected during the most severe phase of cramping, and 82.3 per cent of all specimens obtained during menstruation accompanied by dysmenorrhea, produced responses in which the oxytocic phase was positive. In the four groups of menstrual specimens, the percentages of positive oxytocic effects varied directly with the severity of the symptoms; in the intermenstrual groups, they were essentially equal.

Responses in which only the oxytocic phase was positive (Fig. 4) occurred with greatest frequency (Chart I, cross-hatched portions of graphs) after the injection of urine collected during the most severe phase of dysmenorrhea. Such responses were numerous throughout the cycle in dysmenorrheic women but were relatively infrequent in association with other conditions.

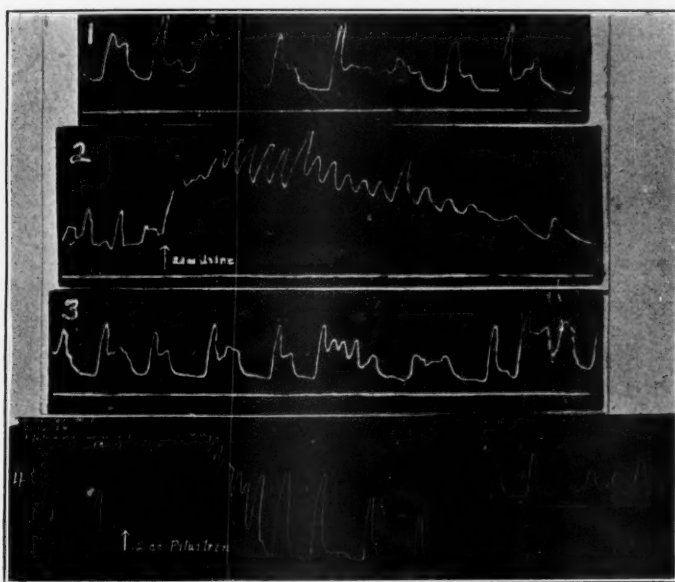


Fig. 4.—Response to urine (Tracing 2) in which the oxytocic phase was positive, the inhibitory phase negative (no reduction in subsequent motility or in response to pituitrin, Tracing 4).

The percentage of positive inhibitory effects was greatest in relation to menstruation accompanied by no cramps (Chart II, complete graphs). The percentages in the menstrual groups were inversely proportional to the severity of the symptoms; in the dysmenorrhea-menstrual groups they were significantly low as compared with all other groups.

Percentages of responses in which only the inhibitory phase was positive (Figs. 5 and 6) varied with the severity of symptoms as follows (Chart II, lined portions of graphs): inversely in the menstrual groups, and directly in the intermenstrual groups. No responses of this type were obtained with dysmenorrhea-menstrual specimens or with urine from men. As compared with all other conditions, the percentage was greatest in relation to menstruation accompanied by no cramps.

Responses in which both phases were positive (Fig. 3) occurred in all groups (Charts I and II, shaded portions of graphs); the percentage was highest in the case of specimens from men. The great majority of positive responses to urine



from men and from nonmenstruating women with no cramps were of this type. Variations in the percentage of positive oxytocic or inhibitory effects in the other groups were dependent chiefly upon variations in the number of responses in which only one phase was positive. This was especially true with respect to differences referable to menstruation and to the intermenstruum, respectively, in each group of women.

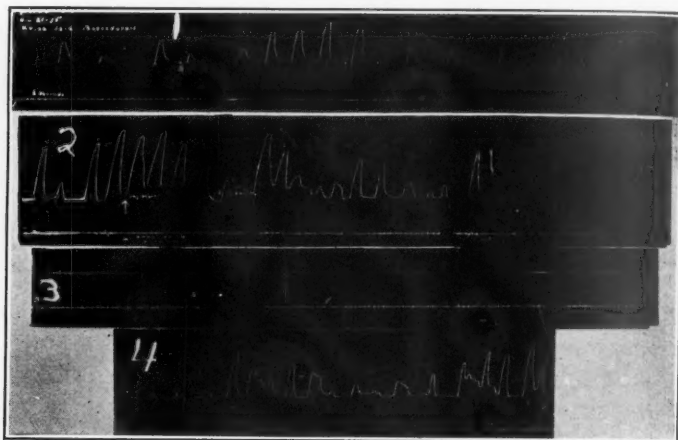


Fig. 5.—Response to urine in which the oxytocic phase was negative, the inhibitory phase positive, as indicated by complete inhibition of rhythmical motility (Tracings 2 and 3). Urine injected at arrow in Tracing 2. Return of motility in Tracing 4.



Fig. 6.—Response to urine in which the oxytocic phase (Tracing 2) was insignificant, the inhibitory phase positive, as indicated by slight gradual reduction in the amplitude of the rhythmical contractions and marked reduction in magnitude of response to pituitrin (Tracing 4) (compare with Fig. 4, Tracing 4).

Results obtained with urine from dysmenorrheic women were the exact reverse of those obtained with urine from women with no cramps with respect to: (1) the nature of effects characteristic of menstruation; and (2) the relation to menstruation and to the intermenstruum, respectively, of positive inhibitory effects and of responses in which *only* the inhibitory effect was positive.

Menstrual and intermenstrual variations in the effects of urine from single individuals were of the nature indicated by the data as presented. There was some indication that effects could be further related to the phases of the intermenstruum; however, it was felt that the present material was insufficient for conclusions on this point. For these reasons, details of results in individual cases have not been presented. It should be noted that cyclic changes were as definite in the women with mild cramps as they were in the other women studied, but they varied in nature in different individuals. This explains the relatively insignificant variations in the percentages of positive oxytocic and inhibitory effects

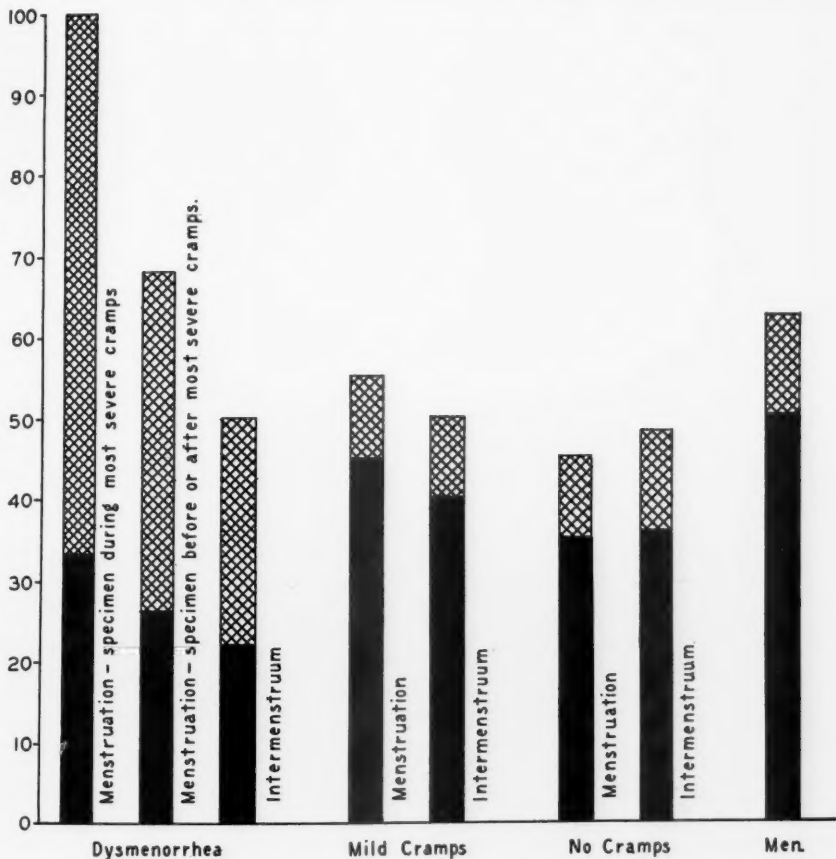


Chart I.—Distribution of positive oxytocic effects, considered separately, in relation to the conditions obtaining at the time of collection of each specimen of urine. *Complete graphs:* Percentage of all specimens in each group producing positive oxytocic effects. *Cross-hatched portions of graphs:* Percentage of all specimens in each group producing responses in which the oxytocic phase was positive, the inhibitory phase absent or insignificant (Fig. 4). *Shaded portions of graphs:* Percentage of all specimens in each group producing responses in which both oxytocic and inhibitory phases were positive (Fig. 3).

in this group. In four of the cases studied, the discomfort experienced at different menstrual periods investigated varied in severity from dysmenorrhea to mild or no cramps. In every instance, the effects of the urine varied accordingly; they were predominantly oxytocic in association with dysmenorrhea, both oxytocic and inhibitory or predominantly inhibitory in association with mild or no cramps.

Pathologic or other special conditions were present in four of the individuals studied. The conditions present and the effects of the urine from these individuals are presented in Table II. It was of interest that after the relief of dysmenorrhea by presacral sympathectomy in one individual, cyclic variations were of the dysmenorrhea type.

#### DISCUSSION

It is apparent from the results obtained that human urine at times contains a substance or substances which affect uterine motility in the unanesthetized rabbit, producing a response in which an initial phase

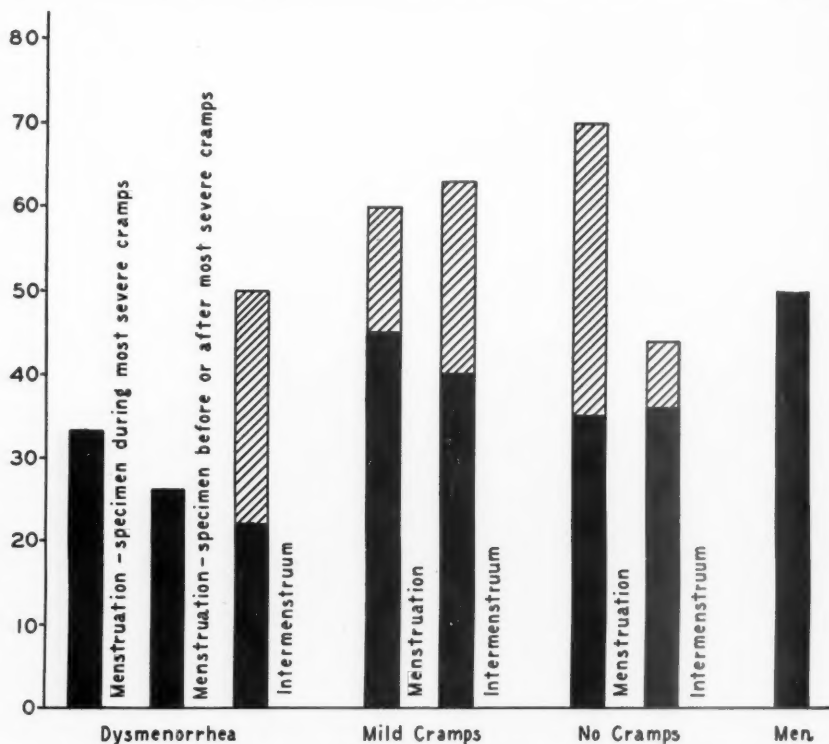


Chart II.—Distribution of positive inhibitory effects, considered separately, in relation to the conditions obtaining at time of collection of each specimen of urine. *Complete graphs:* Percentage of all specimens in each group producing positive inhibitory effects. *Lined portions of graphs:* Percentage of all specimens in each group producing responses in which the inhibitory phase was positive, the oxytocic phase absent or insignificant (Figs. 5 and 6). *Shaded portions of graphs:* Percentage of all specimens in each group producing responses in which both oxytocic and inhibitory phases were positive (Fig. 3).

of contraction is followed by evidence of an inhibitory effect. The responses produced by different specimens of urine from the same individual may vary widely in magnitude; further, the two phases of the response may vary in magnitude independently as well as simultaneously. Independent variations occur chiefly in women, and, with respect to nature and to occurrence in relation to the phases of the menstrual cycle, are definitely related to the degree of menstrual dis-

comfort. Thus, in women without dysmenorrhea, such variations involve chiefly the inhibitory phase, whereas in women with dysmenorrhea, both phases are involved, the oxytocic to a greater degree. Further, independent variations occur throughout the cycle in dysmenorrheic women and, to a less extent, in women with mild cramps, but are largely confined to menstruation in women with no cramps.

Variations in the effects of urine from women, which are chiefly dependent upon independent variations in the two phases of the response, are definitely referable to menstrual and intermenstrual phases of the cycle. The nature of the cyclic changes is further referable to the degree of menstrual discomfort. Thus, in women with no cramps, there is at menstruation an increase in the degree of inhibition produced, with relatively little change throughout the cycle in the oxytocic effect. In women with dysmenorrhea, there is at menstruation an increase in the oxytocic effect, with a concurrent decrease in the degree of inhibition. The two effects tend to vary in inverse ratio throughout the cycle. In women with mild cramps, cyclic changes vary in different individuals.

TABLE II. EFFECTS OF URINE FROM INDIVIDUALS IN WHOM PATHOLOGIC OR OTHER SPECIAL CONDITIONS WERE PRESENT

CONDITION	NO. OF CASES	REMARKS	RESULTS
Essential hypertension	1	Dysmenorrhea of regular occurrence since onset of hypertension; no dysmenorrhea previously. Only one specimen of urine investigated.	The specimen, voided during the most severe phase of cramping, produced a response in which the oxytocic phase was positive, the inhibitory phase negative.
Postoperative (presacral sympathectomy for the relief of dysmenorrhea)	1	The menstrual period investigated began three days after operation, at the normally expected time. No cramps at this period. The specimen was obtained at the time when, previous to operation, cramps had been most severe. Three specimens investigated.	Menstrual specimen produced a response in which the oxytocic phase was positive, the inhibitory phase negative. Two intermenstrual specimens produced responses in which the oxytocic phase was negative or insignificant, the inhibitory phase positive.
Thyroid therapy for relief of dysmenorrhea	1	Urine collected during one complete cycle and parts of preceding and following cycles. Patient took 1 gr. of thyroid daily for 11 days before the onset of the second menstrual period. Dysmenorrhea was present at both periods.	Menstrual and intermenstrual variations in the effects of the urine were similar to those observed in other women with dysmenorrhea.
Spinal arthritis	1	The patient, a man, suffers pain frequently, but none was present at the time specimen was collected.	The specimen produced a response in which both oxytocic and inhibitory phases were positive.

There may be a simultaneous increase in both effects at menstruation, or inhibitory effects may vary independently in relation to the cycle as in patients having no cramps or as in those with dysmenorrhea. In the latter case, corresponding variations in the oxytocic effect are lacking.

The nature of cyclic changes and the relative absence of predominantly oxytocic effects in individuals without dysmenorrhea indicate that dysmenorrhea is definitely associated with a marked oxytocic effect of the urine which is accompanied by relative absence of an inhibitory effect.

No attempt has been made to identify the active principle or principles present in the urine examined. However, the similarity of the effects of urine and of pituitrin is striking. It was shown by Reynolds<sup>17, 19</sup> and by Weinstein and Friedman<sup>20</sup> that the initial contraction produced by pituitrin is due to the oxytocic factor, the subsequent inhibition, to the pressor factor. That the latter is able to reduce the sensitivity of the uterus without necessarily affecting the rhythmical motility was demonstrated by Weinstein and Friedman.<sup>20</sup>

#### CONCLUSIONS

1. Human urine, when injected into rabbits, normally produces a response of the uterus in which an initial phase of contraction is followed by evidence of an inhibitory effect (reduction of spontaneous motility and decrease in the sensitivity of the uterus to pituitrin).
2. Urine excreted during normal menstruation shows an increase in the inhibitory activity, which is inversely proportional to the degree of discomfort present.
3. Urine excreted during dysmenorrheic cramping shows a marked increase in the oxytocic activity, together with a less marked, but significant, decrease in the inhibitory activity.

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## THE USE OF PARATHYROID EXTRACT IN THE CONTROL OF EARLY NAUSEA AND VOMITING OF PREGNANCY\*

### A PRELIMINARY REPORT

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NAUSEA and vomiting are generally considered necessary accompaniments of early pregnancy and must be tolerated in varying severity until life is felt. According to Stander<sup>1</sup> this vomiting occurs in 50 per cent of all pregnancies. Our records indicate that vomiting might begin as early as the first week of gestation; however, it usually commences during the second week. This syndrome is characterized by slight or moderate nausea and is most often associated with the vomiting of a bile-stained foamy fluid, following which the patient immediately feels a sense of relief. The nausea and vomiting usually last for three and a half to four and a half months but occasionally persist throughout gestation. In cases where this mild type of toxemia does not abate the condition may gradually progress to the more severe types of toxemia.<sup>†</sup> Strauss<sup>2</sup> aptly emphasized that the vomiting of early pregnancy is never a physiologic process, but is the expression of some pathologic state whether neurotic or toxic, always dangerous and threatening.

### PATHOLOGY

The similarity of the pathologic lesions in hyperemesis to those of eclamptic toxemia have been pointed out by Ewing<sup>3</sup> who demonstrated that in both situations the fundamental lesion is necrosis of the liver cells. Some observers have contrasted the central lobule necrosis seen in cases of vomiting in pregnancy with the peripheral zone necrosis of eclampsia, and have considered this pathologic difference to be indicative of an etiological difference. Davidson,<sup>4</sup> however, discussing the pathology of eclampsia and puerperal toxemia, states that in some instances of severe toxemia there is involvement of the peripheral zones, in others widespread central and midzone necrosis, and in still others no gross hepatic lesions but only small areas of focal necrosis. This demonstrates, we believe, that the location of the lesion in the liver is of no diagnostic significance in differentiating the types of

\*Read at a meeting of the Obstetrical Society of Philadelphia, October 1, 1936.

This study was aided by a grant from the Jubilee Fund of King Solomon Lodge 279 F. and A. M. of New York State.

<sup>†</sup>The following classification of toxemias is given by Stander:<sup>1</sup> (1) vomiting of pregnancy, (2) low reserve kidney, (3) nephritis complicating pregnancy, (4) pre-eclampsia, (5) eclampsia, and (6) acute yellow atrophy of the liver.

toxemia. Ewing<sup>3</sup> also noted that the location of the lesion did not disclose the severity of the symptoms. It would seem, therefore, that the underlying disturbance for the milder intoxication of pregnancy, namely vomiting, is probably a lesion in the liver similar to but of a milder degree than that seen in the more severe forms of toxemia of pregnancy.

#### ETIOLOGY

Numerous theories have been advanced regarding the etiology of this vomiting, varying to include maternal, fetal, placental, endocrine, chemical, and dietary disturbances. We feel that it is beyond the scope of this paper to discuss the all too many conflicting points of view regarding the etiology of this condition, but shall confine ourselves to those having a direct bearing on the problem at hand. Whether disturbances in the carbohydrate metabolism exist or are of primary etiologic significance is not clear. The opinions regarding this are conflicting. That treatment with glucose, however, is beneficial in many cases of vomiting can be undisputed. It is possible that an altered carbohydrate metabolism may be dependent on a primary liver damage similar to the carbohydrate disturbance found by Minot and Cutler<sup>5</sup> in their dogs where liver damage was produced by carbon-tetrachloride poisoning. In this latter situation the liver lesion is similar to that occurring in the toxemias of pregnancy. It has also been demonstrated in phosphorous poisoning that there is a disappearance of glycogen from the liver which can be replenished by sugar feeding. And furthermore, the toxic manifestations of carbontetrachloride poisoning can likewise be relieved by sugar therapy. It would seem, therefore, by analogy that high carbohydrate feeding would be indicated in the toxemias of pregnancy where liver damage is also present.

Much has been written regarding the alterations of calcium metabolism both in the normal and in the toxemic states of pregnancy. From the large mass of conflicting data, Stander<sup>1</sup> states that one cannot conclude that a decrease in the total blood calcium or in the dialyzable blood calcium is associated with eclampsia. These blood findings, however, do not necessarily reveal the complete story regarding the calcium metabolism. It has been frequently demonstrated that the level of calcium in the blood does not parallel the degree of calcium retention in the tissues. Calcium has been advocated in the treatment of the toxemias of pregnancy. The rationale for the use of this salt is dependent upon the finding by many observers of a lowered blood calcium in eclampsia and upon the analogy that convulsions occur both in eclampsia and in the hypocalcemia of tetany. But, as mentioned above by Stander, lowering of the blood calcium is not a consistent finding in eclampsia or in the other toxemias and, therefore, any bene-

ficial effect of calcium therapy in the intoxications of pregnancy might have an influence aside from restoring the blood calcium to a normal level. A relationship between the disturbances in calcium metabolism and carbohydrate metabolism has been demonstrated in many ways. Minot and Cutler<sup>5</sup> found that the hypoglycemia associated with the liver damage produced by carbontetrachloride poisoning was relieved when calcium was administered. These authors quote Underhill and Blatherwick<sup>6</sup> as having demonstrated a hypoglycemia following parathyroidectomy where the blood sugar was raised by calcium therapy. The relief of the hypoglycemia and other symptoms of intoxication from carbontetrachloride poisoning by calcium therapy observed by the above-mentioned authors occurred even though there was no evidence of a reduced blood calcium during the toxic state. Since the liver pathology in the vomiting of pregnancy, where central necrosis if found, is similar to that described for carbontetrachloride poisoning, it would seem that a beneficial action of calcium therapy in the former situation would be similar to its effect in carbontetrachloride poisoning, that is, an influence on the carbohydrate metabolism.

It is understandable, in the light of recent work, why calcium therapy has been of so little value in the convulsions of eclampsia. It is known that the normal response of an animal to parathyroid administration is a rise in the blood calcium. This rise, as Nitzescu<sup>7</sup> has shown, is greatly diminished in the presence of liver damage produced by phosphorous poisoning. Greenberg<sup>8</sup> found a similar but less striking failure of the blood calcium to rise after parathormone administration when liver damage was produced with hydrazine. It would therefore appear that the liver damage as seen in the toxemias of pregnancy might interfere not only with the carbohydrate but also with the calcium metabolism of the body. The normal influence of the parathyroid gland in maintaining a proper balance of calcium in the body may not be operative in these circumstances of liver damage.

Calcium therapy alone, and this has likewise been Nixon's<sup>9</sup> experience, was not greatly beneficial in the treatment of the vomiting in pregnancy. *Since calcium therapy alone was ineffectual in relieving the symptoms of this intoxication, and since, as Nitzescu<sup>7</sup> observed, the normal action of the parathyroid gland is disturbed during liver damage, it occurred to us that a combination of calcium and parathyroid extract, where these two substances could be supplied in amounts larger than usual to the tissues, might be of value in the treatment of this mild intoxication.* Further study confirmed this supposition. Lopez,<sup>10</sup> using parathyroid hormone in the treatment of eclampsia, noted the disappearance of the toxic symptoms as well as the convulsions following its use. As far as we can determine, this therapy has not been heretofore applied to the mild toxemias.

## EXPERIMENTAL DATA

The patients in this study were divided into two groups. All patients in both groups were placed on a diet high in carbohydrates, low in fat, and with restricted condiments. The patients in Group I were given orally about 40 gr. of calcium daily, usually in the form of phosphate, 10 c.c. of a 10 per cent solution of calcium gluconate intravenously at varying intervals. The patients in Group II were given the calcium orally and 100 units of parathyroid extract in some cases intramuscularly and in others intravenously every two or three days. A few of the patients in the second group were also given calcium gluconate parenterally.

Since these patients were from private practice, it was difficult in many of them to get full cooperation. In the first place, many of them reported after vomiting had been established for many days and often were unable to recall accurately how long nausea and vomiting had existed. Second, it was difficult to get them to come in for injections at frequent intervals. Third, it was not possible to determine

TABLE I

CASE	GRAVIDA	AGE OF PREGNANCY IN DAYS WHEN FIRST SEEN (M.L. TO FIRST VISIT)	DAY OF PREGNANCY VOMITING CEASED	LENGTH IN DAYS OF SYMPTOMATOLOGY FOLLOWING ONSET OF TREATMENT	NO. OF CALCIUM GLUCONATE INJECTIONS
JL-1	ii	47 days	61st day	14 days	4 each 10 c.c.
SM-2	ii	78 days	94th day	16 days	7 each 10 c.c.
SS-3	i	67 days	110th day	43 days	6 each 10 c.c.
LS-4	i	71 days	78th day	7 days	4 each 10 c.c.
EB-6	i	110 days	200th day	90 days	9 each 10 c.c.
MK-7	i	104 days	124th day	20 days	2 each 10 c.c.
RK-8	i	74 days	83rd day	9 days	3 each 10 c.c.
CK-9	ii	66 days	76th day	10 days	2 each 10 c.c.
RS-10	i	72 days	95th day	23 days	5 each 10 c.c.
DG-11	i	56 days	114 days	58 days	11 each 10 c.c.
BC-12	i	47 days	89th day	42 days	4 each 10 c.c.
EI-13	i	56 days	90th day	34 days	11 each 10 c.c.

*First and Second Months*

JL-1	ii	47 days	61st day	14 days	4 each 10 c.c.
DG-11	i	56 days	114 days	58 days	11 each 10 c.c.
BC-12	i	47 days	89th day	42 days	4 each 10 c.c.
EI-13	i	56 days	90th day	34 days	11 each 10 c.c.

*Third and Fourth Months*

SM-2	ii	78 days	94th day	16 days	7 each 10 c.c.
SS-3	i	67 days	110th day	43 days	6 each 10 c.c.
LS-4	i	71 days	78th day	7 days	4 each 10 c.c.
RK-8	i	74 days	83rd day	9 days	3 each 10 c.c.
CK-9	ii	66 days	76th day	10 days	2 each 10 c.c.
RS-10	i	72 days	95th day	23 days	5 each 10 c.c.
EB-6	i	110 days	200th day	90 days	9 each 10 c.c.
MK-7	i	104 days	124th day	20 days	2 each 10 c.c.

TABLE II

CASE	GRAVIDA	AGE OF PREG- NANCY IN DAYS WHEN FIRST SEEN (M.L. TO FIRST VISIT)	DAY OF PREGNANCY VOMITING CEASED	LENGTH IN DAYS OF SYMPTOM- ATOLOGY FOLLOWING ONSET OF TREATMENT	NO. OF PARATHYROID EXTRACT INJECTIONS GIVEN
<i>First and Second Months</i>					
BJ-1	i	51 days	61st day	10 days	5 each 1 c.e.
LS-2	i	61 days	78th day	17 days	4 each 1 c.e.
JF-3	i	52 days	60th day	8 days	1 each 1 c.e.
MK-4	ii	56 days	67th day	11 days	3 each 1 c.e.
RG-5	i	55 days	78th day	23 days	10 each 1 c.e.
RG-6	ii	52 days	58 days	6 days	3 each 1 c.e.
JF-7	i	60 days	70 days	10 days	4 each 1 c.e.
SL-8	i	55 days	77 days	22 days	6 each 1 c.e.
ES-9	i	49 days	52nd day	3 days	3 each 1 c.e.
CL-10	i	50 days	78th day	28 days	12 each 1 c.e.
OL-11	ii	36 days	71st day	35 days	7 each 1 c.e.
ES-12	i	51 days	67th day	16 days	2 each 1 c.e. 2 cal. gluc.
EN-13	i	53 days	55 days	2 days	2 each 1 c.e.
MT-14	i	42 days	57 days	15 days	2 each 1 c.e. 2 cal. gluc.
TM-15	i	34 days	38 days	4 days	3 each 1 c.e.
HD-16	i	59 days	67th day	8 days	2 each 1 c.e.
RC-17	i	64 days	87th day	23 days	6 each 1 c.e.
EC-18	i	36 days	38th day	2 days	1 each 1 c.e. 1 cal. gluc.
BS-19	i	40 days	46th day	6 days	4 each 1 c.e.
MP-20	i	44 days	68 days	24 days	5 each 1 c.e.
GG-21	i	54 days	92 days	38 days	7 each 1 c.e. 7 cal. gluc.
SM-22	i	40 days	56th day	16 days	4 each 1 c.e.
SS-23	i	62 days	79th day	17 days	7 each 1 c.e.
EG-24	iii	41 days	64th day	23 days	8 each 1 c.e.
SF-25	i	54 days	84th day	30 days	6 each 1 c.e.
ET-26	i	54 days	68th day	14 days	8 each 1 c.e.
AC-27	ii	55 days	57 days	2 days	2 each 1 c.e.
SC-28	ii	50 days	57 days	7 days	7 each 1 c.e.
LV-29	i	51 days	72nd day	21 days	6 each 1 c.e.
AC-30	i	54 days	60th day	6 days	3 each 1 c.e.
NF-31	i	66 days	70th day	4 days	3 each 1 c.e.
MA-32	ii	44 days	85th day	41 days	14 each 1 c.e.
EY-33	i	41 days	61st day	20 days	3 each 1 c.e.
PB-34	i	62 days	96 days	34 days	9 each 1 c.e. 9 cal. gluc.
CG-35	ii	45 days	58 days	13 days	3 each 1 c.e.
CP-36	ii	43 days	57 days	14 days	3 cal. gluc. 2 each 1 c.e.
HG-37	i	49 days	53 days	4 days	4 cal. gluc. 3 each 1 c.e.
RB-38	i	51 days	59 days	8 days	3 cal. gluc. 3 each 1 c.e.
LR-39	ii	52 days	59 days	7 days	3 cal. gluc. 2 each 1 c.e.
HO-40	i	63 days	80 days	17 days	3 cal. gluc. 6 each 1 c.e.
JF-41	i	41 days	43 days	2 days	4 cal. gluc. 2 each 1 c.e.
GK-42	i	53 days	59 days	6 days	2 cal. gluc. 2 each 1 c.e. 2 cal. gluc.



TABLE II—CONT'D

CASE	GRAVIDA	AGE OF PREG- NANCY IN DAYS WHEN FIRST SEEN (M.L. TO FIRST VISIT)	DAY OF PREGNANCY VOMITING CEASED	LENGTH IN DAYS OF SYMPTOM- ATOLOGY FOLLOWING ONSET OF TREATMENT	NO. OF PARATHYROID EXTRACT INJECTIONS GIVEN
<i>First and Second Months—Cont'd</i>					
SG-43	i	15 days	18 days	3 days	3 each 1 c.c. 3 cal. gluc.
RS-44	i	42 days	44 days	2 days	2 each 1 c.c. 2 cal. gluc.
JS-45	ii	42 days	44 days	2 days	1 each 1 c.c. 1 cal. gluc.
RH-46	i	63 days	67 days	4 days	4 each 1 c.c. 4 cal. gluc.
SL-47	i	61 days	66 days	5 days	5 each 1 c.c. 5 cal. gluc.
SL-48	i	55 days	57 days	2 days	2 each 1 c.c. 2 cal. gluc.
RF-49	ii	56 days	61 days	5 days	4 each 1 c.c. 4 cal. gluc.
RL-50	i	61 days	64 days	3 days	3 each 1 c.c. 3 cal. gluc.
PM-51	i	58 days	60 days	2 days	2 each 1 c.c. 2 cal. gluc.
<i>Third and Fourth Months</i>					
FG-52	i	65 days	88 days	23 days	9 each 1 c.c.
SL-53	i	81 days	90th day	9 days	5 each 1 c.c.
RA-54	i	61 days	75th day	14 days	4 each 1 c.c.
EL-55	i	125 days	157th day	32 days	9 each 1 c.c.
FF-56	ii	127 days	129 days	2 days	1 each 1 c.c.
EN-57	ii	77 days	86 days	9 days	5 each 1 c.c.
VK-58	i	92 days	94th day	2 days	1 each 1 c.c. 1 cal. gluc.
SC-59	i	109 days	118 days	9 days	4 each 1 c.c.
CR-60	i	105 days	113 days	8 days	4 each 1 c.c.
MP-61	i	78 days	92 days	14 days	5 each 1 c.c.
RL-62	i	69 days	116th day	47 days	13 each 1 c.c.
HC-63	i	65 days	71st day	6 days	4 each 1 c.c.
RZ-64	i	48 days	70 days	22 days	11 each 1 c.c.
RO-65	i	73 days	95th day	22 days	16 each 1 c.c.
RR-66	i	91 days	111th day	20 days	6 each 1 c.c.
IB-67	i	110 days	113 days	3 days	3 each 1 c.c.
AL-68	i	74 days	81 days	7 days	3 each 1 c.c.
SP-69	ii	67 days	70th day	3 days	2 each 1 c.c.
MM-70	i	110 days	128th day	18 days	4 each 1 c.c.
MR-71	ii	89 days	94th day	5 days	3 each 1 c.c.
RB-72	ii	81 days	92 days	11 days	3 each 1 c.c. 4 cal. gluc.
VB-73	ii	94 days	96 days	2 days	2 each 1 c.c.
FE-74	i	75 days	79 days	4 days	2 each 1 c.c. 2 cal. gluc.
ET-75	i	86 days	95th day	9 days	7 each 1 c.c. 5 cal. gluc.
ES-76	i	73 days	75 days	2 days	2 each 1 c.c. 2 cal. gluc.
AB-77	ii	72 days	77th day	5 days	2 each 1 c.c. 2 cal. gluc.
EH-78	v	72 days	76th day	4 days	2 each 1 c.c.
DW-79	i	118 days	121 days	3 days	4 each 1 c.c. 4 cal. gluc.

TABLE II—CONT'D

CASE	GRAVIDA	AGE OF PREGNANCY IN DAYS WHEN FIRST SEEN (M.L. TO FIRST VISIT)	DAY OF PREGNANCY VOMITING CEASED	LENGTH IN DAYS OF SYMPTOMATOLOGY FOLLOWING ONSET OF TREATMENT	NO. OF PARATHYROID EXTRACT INJECTIONS GIVEN
<i>Third and Fourth Months—Cont'd</i>					
FZ-80	i	71 days	74th day	3 days	2 each 1 c.c.
EG-81	i	67 days	74 days	7 days	3 each 1 c.c. 3 cal. gluc.
PB-82	i	89 days	92 days	3 days	3 each 1 c.c. 3 cal. gluc.
RS-83	i	88 days	90 days	2 days	3 each 1 c.c. 3 cal. gluc.
FM-84	i	70 days	72 days	2 days	2 each 1 c.c. 2 cal. gluc.
PS-85	ii	103 days	107 days	4 days	3 each 1 c.c. 3 cal. gluc.
PL-86	i	77 days	81 days	4 days	3 each 1 c.c. 3 cal. gluc.
BF-87	i	89 days	91 days	2 days	2 each 1 c.c. 2 cal. gluc.
DR-88	i	78 days	84 days	6 days	6 cal. gluc. 6 each 1 c.c.

accurately how much calcium they actually took by mouth. In general, however, the patients cooperated very well in this study.

A summary of the results of the twelve patients in the first group is given in Table I. Table II is a summary of the 88 patients in Group II. The data presented in Tables I and II demonstrated the superiority of parathyroid extract plus calcium over calcium alone and over the usual accepted therapy. The tables clearly indicate a definite shortening of the duration of the early vomiting of pregnancy by this treatment. Whereas in Group I (Table I), the nausea and vomiting persisted on an average of 30.5 days after treatment was instituted with an average of 101 days in pregnancy, Group II, Table II, where parathyroid extract was used along with calcium the symptoms persisted on an average of only 11.2 days with an average of 76 days in preg-

TABLE III A. COMPARATIVE FIGURES OF TABLES I AND II (FIRST AND SECOND MONTHS OF PREGNANCY)

	NUMBER OF CASES	AGE OF PREGNANCY IN DAYS WHEN FIRST SEEN (M.L. TO FIRST VISIT)	DAY OF PREGNANCY VOMITING CEASED	LENGTH IN DAYS OF SYMPTOMATOLOGY FOLLOWING ONSET OF TREATMENT	NUMBER OF INJECTIONS
Calcium gluconate	4	51.5	88.5	37.0	7.5
Parathyroid extract	51	50.5	63.2	12.7	4.3

TABLE III B. COMPARATIVE FIGURES OF TABLES I AND II (THIRD AND FOURTH MONTHS OF PREGNANCY)

	NUMBER OF CASES	AGE OF PREG- NANCY IN DAYS WHEN FIRST SEEN (M.L. TO FIRST VISIT)	DAY OF PREGNANCY VOMITING CEASED	LENGTH IN DAYS OF SYMPTOM- ATOLOGY FOLLOWING ONSET OF TREATMENT	NUMBER OF INJECTIONS
Calcium gluconate	8	80.3	107.5	27.2	4.5
Parathyroid extract	37	84.3	93.7	9.4	4.4

TABLE III C. COMPARISON OF ENTIRE TABLE I AND ENTIRE TABLE II

	NUMBER OF CASES	AGE OF PREGNANCY IN DAYS WHEN FIRST SEEN	DAY OF PREGNANCY VOMITING CEASED	LENGTH IN DAYS OF SYMPTOM- ATOLOGY FOLLOWING ONSET OF TREATMENT	NUMBER OF INJECTIONS
Calcium gluconate	12	70.6	101	30.5	5.7
Parathyroid extract	88	64.8	76	11.2	4.5

nancy. In Group II there were three patients who were not included in the latter tables; in these the parathyroid extract and calcium failed to control the vomiting.

#### THREE CASES NOT RESPONDING TO ANY TYPE OF TREATMENT

##### KY-SPECIAL I.—

*Physical Examination:* Primigravida, aged twenty-six years, married four years, weight 114 pounds, height 5 feet 4 inches, heart and lungs negative, pelvic measurements normal. Wassermann negative.

*Menstrual History:* Thirteen  $\frac{35 \text{ day}}{6-7 \text{ day}}$  slight pain lower abdomen few days before and stops with onset; moderate flow, mostly second day, no clots. Last menstrual period October 16. Due: July 23.

*Personal History:* No miscarriages, tonsils and adenoids removed in childhood, pelvic abscess operation.

*Present Complaints:* (1) Nausea and vomiting (three times a day), (2) burning feeling and bitter taste in mouth, (3) frequent urination, and (4) best weight 113 pounds.

*Vaginal Examination:* Primiparous vagina, uterus enlarged commensurate with period of amenorrhea.

*Summary of Prenatal Care.*—(1) Urine for last five months of pregnancy at times showed a trace of albumin and occasional hyaline cast. (2) Blood pressure varied from  $\frac{120 \text{ to } 128 \text{ systolic}}{80 \text{ to } 90 \text{ diastolic}}$ . (3) Increase in weight 18 pounds, gain regular without losses. (4) Fifteen injections (1 c.c. each) of parathyroid extract given. (5) All types of treatment given. (6) Calcium taken irregularly. Patient felt no medicine or food agreed with her. (7) Delivered of a male child.

*NR-SPECIAL II.—*

*Physical Examination:* Multipara ii, aged thirty years, married seven years, two pregnancies; instrumental; weight 122½ pounds, height 5 feet 5¼ inches, blood pressure 110/80, pelvic measurements normal, Wassermann, chemistry and blood count normal.

*Menstrual History:* Twelve  $\frac{28 \text{ days}}{3 \text{ days}}$  no pain, scant flow, mostly second day, small clots occasionally, last menstrual period April 4. Due: January 9.

*Personal History:* Diphtheria early childhood, scarlet fever at nineteen years of age, appendix out 1924, second child died at nine months of age (pneumonia?).

*Present Complaints:* (1) Nausea and vomiting, (2) moderately constipated, (3) restless, (4) headaches off and on, and (5) best weight 125 to 128 pounds.

*Vaginal Examination:* Rectocele, cystocele, lacerated cervix, uterus enlarged commensurate with period of amenorrhea.

*Summary of Prenatal Care:* (1) Urine negative throughout pregnancy. (2) Blood pressure varied from  $\frac{100 \text{ to } 120 \text{ systolic}}{70 \text{ to } 80 \text{ diastolic}}$ . (3) Increase in weight 14¾ pounds, gain was regular without any losses. (4) Nine injections parathyroid extract given. (5) All known effective home treatment given. (6) Vomiting aggravated at approximately time of month that period would have been due. (7) Delivered of male child.

*RR-SPECIAL III.—*

*Physical Examination:* Primigravida, aged twenty-two years, married one and one-half years, height 5 feet 4½ inches, weight 116 pounds, blood pressure 110/70, acne vulgaris of face, eyes refracted, lungs negative, heart—aortic systolic murmur referred to vessels right side of neck, pelvic measurements normal. Wassermann negative.

*Menstrual History:* Thirteen  $\frac{7 \text{ to } 8 \text{ weeks}}{8 \text{ days}}$  until marriage  $\frac{28 \text{ days}}{6 \text{ days}}$ . Occasional cramps in lower abdomen, moderate to profuse flow mostly second and fourth days, small clots. Last menstrual period June 26. Due: April 2.

*Personal Examination:* No miscarriages, tonsils out age nine years, cystic ovary (according to previous examination by physician).

*Present Complaints:* (1) Nausea and vomiting, (2) frequent urination, and (3) cramps July 1, no bleeding.

*Vaginal Examination:* Primiparous vagina, uterus enlarged commensurate with period amenorrhea.

*Summary of Prenatal Care:* (1) Urine normal throughout. (2) Blood pressure varied from  $\frac{100 \text{ to } 122 \text{ systolic}}{60 \text{ to } 80 \text{ diastolic}}$ . (3) Increased weight 23½ pounds, gained regularly up to fourth month, then lost three pounds, thereafter gained regularly until delivery. (4) Twenty injections parathyroid extract. (5) Nauseated for two weeks after life was felt, morning nausea until term. (6) Calcium taken irregularly, nausea less when injection parathyroid extract was taken. (7) Delivered of female child.

## CONCLUSIONS AND SUMMARY

From the data presented it seems fair to conclude that parathyroid extract along with calcium therapy is of distinct value in controlling the early nausea and vomiting of pregnancy. From experimental data there is a rationale for the use of this extract. Whether, as suggested by Lopez,<sup>10</sup> parathyroid extract will be of value in the late toxemias of pregnancy can be demonstrated only by future investigation. In presenting this treatment of the early toxemias with parathyroid ex-

tract, we do not wish to create the impression that we feel that other sound therapeutic measures should be neglected in the handling of such patients but we offer this as an additional therapeutic procedure.

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## DISCUSSION

DR. JOHN MCGLINN.—Many of the cases which show not the ordinary nausea of pregnancy but the true hyperemesis of the early months of pregnancy, do develop the toxemia of the later months. Dr. Missett presented a series of cases several years ago, showing a greater than average incidence of toxemia among the cases which had had marked hyperemesis in the early stages of pregnancy.

We have all tried the various forms of treatment for nausea and vomiting of the early months of pregnancy. We were enthralled, for example, at one time with the use of corpus luteum, a most irrational treatment. Yet I know from the full series of cases which Sussman has studied that he has undoubtedly added something in the combination of calcium and parathyroid in the treatment of this condition which is of distinct value. The treatment he has presented deserves a trial by the members of this Society.

DR. COLLIN FOULKROD.—Are we to gather from this paper that the lowering of the calcium of the blood will lead to eclampsia if allowed to go untreated? The lowered calcium in the blood is replenished, as I understand it, by the action of parathyroid hormone drawing the calcium from the body stores. This hormone does not absorb or help introduce new calcium into the tissues. Calcium is absorbed by the action of vitamin D and a normal balance is maintained by carrying off the excess in urine and feces.

From some writings I am led to believe that the use of parathyroid hormone in too large quantities might lead to a *drawing-off* of the calcium from the bones in too great quantity. Yet if you can give an active supply in the food while giving parathyroid hormone, it is quite likely there will be no over-reduction in the bones and other parts of the body of the woman.

I do not believe corpus luteum was a failure in the treatment of nausea of pregnancy. Certain patients need thyroid extract, or extract of corpus luteum to become pregnant, and some also need these glandular extracts throughout pregnancy so that they may continue to full term. Individuals vary in their requirements, and there are a number who are promptly relieved by the use of corpus luteum in the toxemia of pregnancy.

A better form of control would compare the bed day results of the glucose injection method or a modified Titus treatment, and the parathyroid method, to see if the days in bed could be lessened by this proposed new method. We all know that those patients who go to a hospital and accept a modified form of sedative and glucose therapy can be relieved in a few days.



DR. LEON ISRAEL.—I would like to ask Dr. Sussman if he knows if any abnormal reaction from the use of parathyroid and calcium has been reported, and whether, after withdrawal of the treatment, there was any recurrence of nausea and vomiting?

DR. SUSSMAN (closing).—No abnormal reaction has been noted in my cases. A standardized parathyroid extract has been used throughout. In the cases of calcium gluconate the injected material was produced by a fermentative instead of the chemical method. Except in the intractable cases mentioned there was no recurrence of nausea and vomiting.

The hormonal effect of parathyroid extract is stressed in this thesis, which is of a different nature from that usually attributed to calcium and vitamin "D" relationship. There were no bed cases included in this report.

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### A CHEMICAL TEST FOR PREGNANCY APPLIED TO THE DETERMINATION OF ESTRIN IN THE URINE OF NORMAL AND TOXEMIC PATIENTS IN THE LAST TRIMESTER OF PREGNANCY

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THERE are widely divergent opinions concerning the levels of estrin in blood and urine in the late toxemias of pregnancy. Smith and Smith<sup>8-11</sup> found a tendency toward low estrin levels in the blood and urine. Heim<sup>2</sup> obtained values much greater than normal for estrin excretion in the urine in a small series of cases. Bickenbach and Fromme<sup>1</sup> found normal estrin values in the blood, while Runge and Diethelm<sup>4</sup> showed a lowered estrin excretion in the urine in their small series of cases of the late toxemias. All of these estimations were based on bio-assay methods.

Since it was desired to eliminate as many as possible of the variable biologic factors, a chemical test for pregnancy, described by Schmulovitz and Wylie,<sup>6</sup> was used in this investigation of estrin excretion in the urine of patients suffering from the late toxemias of pregnancy. By means of this test we have been able to establish levels of estrin excretion in normal late pregnancy, and also to show a definite lowering of these levels in chronic nephritis complicating pregnancy, and in preeclampsia.<sup>†</sup>

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Received for publication, October 14, 1936.

†The absence of a universally accepted classification of the toxemias of pregnancy is a hindrance to proper correlation of the observations of various workers in this field. It is for this reason that we must give the classification of the late toxemias of pregnancy as accepted in our clinic. By the term late toxemias of pregnancy we refer to: preeclampsia, eclampsia, and chronic nephritis complicating pregnancy. With Irving<sup>3</sup> we agree that preeclampsia should not be subdivided into a mild and severe group. This is at variance with Stander<sup>12,13</sup> who divides the so-called preeclamptic toxemia into "low reserve kidney" and preeclampsia. Thus we have included under the heading of preeclampsia all cases which, in Stander's classification would be subdivided into "low reserve kidney" and preeclampsia.

## METHODS

On all patients frequent examinations were made of blood pressure, eyegrounds, blood chemistry, urine, and kidney function.

Complete mixed twenty-four-hour urine specimens were collected and refrigerated until extracted.

There was no attempt to select the cases for study. Urine specimens were obtained as the patients, not in labor, but in the last trimester of pregnancy, were admitted to the University Hospital. Therefore, the normal controls were scattered among the toxemic cases.

Most patients were service cases; few private cases were included. Nearly all patients reported to our prenatal clinic for from one to six months previous to admission to the hospital.

No cases of true eclampsia appear in this series because of their incontinence which rendered impossible the collection of complete twenty-four-hour urine specimens.

## PROCEDURE

The test devised by Schmulovitz and Wylie<sup>6</sup> for the chemical diagnosis of pregnancy by the detection of estrin in the urine was used in all the cases in this series. The reader is referred to their original paper for full details. Briefly their method "... consists in the extraction of estrin from the urine with ether and its detection by coupling with diazotized para-nitroaniline to form a deep-colored azo dye. . . ."<sup>6</sup> In our procedure certain modifications were made in the original technic, as follows:

1. The urine specimens were hydrolyzed at pH 2 instead of pH 4. This was done because it was felt that there was more complete hydrolysis at pH 2.
2. The specimens were evaporated to 400 c.c. rather than to 200 c.c. This was made possible by using a new type, and larger, extraction flask, resulting in a saving of time.
3. The urines were ether-extracted at pH 2 rather than at pH 1 because it was found by Schmulovitz<sup>5</sup> that further acidification beyond that of hydrolysis gave no increased yields of hormone.
4. After completion of the steam distillation to remove the volatile phenols, the hormone residue was obtained by partial vacuum distillation, instead of removing the water by heating in a glycerin bath at 160° C., because of the time thus saved.

The procedure otherwise was as outlined in the original paper.<sup>6</sup> An improved combined extractor and extract-washer, as described in a later publication by Wylie and Schmulovitz,<sup>14</sup> was used in all our experiments. Each specimen in this entire series was subjected to exactly the same procedure.

The "ferrie chloride number" (F.N. as shown in Tables I to V) is obtained as follows: the final colored alcoholic layer containing the estrin extracted from the specimen is filtered into a colorimeter cup and set at 10 mm., and is compared with a standard 33 per cent ferrie chloride solution, the reading of which is the "ferrie chloride number." A F.N. of 25 or more is considered by Schmulovitz and Wylie<sup>6</sup> as posi-

tive for pregnancy. These investigators<sup>7</sup> ultimately hope to correlate their chemical test and the biologic assays by converting "ferrie chloride numbers" into milligrams of estrin and rat units. This work is in progress.

## DISCUSSION

In Tables I to III the data are arranged under the following headings: case number, age, color, parity of the patient, duration of pregnancy in weeks at the time when the twenty-four-hour specimen of urine

TABLE I. TWENTY-ONE NORMAL CASES

CASE NO.	AGE	COLOR	PARITY	DURATION OF PREG. WHEN URINE OBT.	F.N.	BABY
29	21	W	0-0-0-0	36	152.0	F.T.L.
25	21	W	0-0-0-0	38	112.5	F.T.L.
34	31	B	9-0-4-9	36	112.0	F.T.L.
43	25	W	1-0-0-1	40	98.0	F.T.L.
28	38	W	9-0-0-9	40	97.6	F.T.L.
38	15	B	0-0-0-0	40	96.0	F.T.L.
52	33	W	7-0-1-7	40	94.0	F.T.L.
56	23	W	2-0-0-2	40	93.5	F.T.L.
41	38	B	2-0-0-2	34	92.0	F.T.L.
46	36	B	4-0-0-4	37	86.0	F.T.L.
21	25	B	1-1-3-1	28	78.5	F.T.L.
54	32	B	1-0-0-1	22	76.5	F.T.L.
7	42	B	3-0-0-1	40	67.6	F.T.L.
3	32	W	2-0-1-2	30	66.0	F.T.L.
6	30	W	1-0-0-1	39	66.0	F.T.L.
14	40	W	6-0-0-6	36	64.4	F.T.L.
2	17	W	0-0-0-0	38	64.0	F.T.L.
1	17	W	0-0-0-0	30	60.0	F.T.L.
16	22	W	1-0-0-1	39	59.2	F.T.L.
15	20	B	3-0-0-1	39	57.6	F.T.L.
4	17	W	0-0-0-0	34	56.6	F.T.L.

TABLE II. NINETEEN CASES OF CHRONIC NEPHRITIS COMPLICATING PREGNANCY

CASE NO.	AGE	COLOR	PARITY	DURATION OF PREG. WHEN URINE OBT.	F.N.	BABY
39	34	W	2-0-0-2	40	64.0	F.T.L.
42	36	B	8-0-0-6	40	60.0	F.T.L.
53	45	B	7-0-3-6	40	59.5	F.T.L.
62	43	W	15-0-4-12	38	57.2	F.T.L.
31	21	W	0-1-0-0	33	56.0	36L
55	25	W	0-0-0-0	40	55.0	F.T.L.
33	44	W	8-0-2-8	34	54.5	36D
51	19	W	0-1-0-1	34	52.5	37L
12	49	B	4-0-3-3	38	52.4	F.T.L.
30	21	W	0-1-0-0	30	52.0	36L
44	34	B	3-0-0-3	34	51.0	F.T.L.
58	27	B	2-0-1-2	38	51.0	F.T.L.
50	19	W	0-1-0-1	37	49.0	37L
47	37	B	12-0-0-12	32	48.5	32L
32	36	B	7-0-0-6	40	48.0	F.T.L.
26	32	B	3-0-3-3	40	44.0	F.T.L.
13	36	W	8-0-0-8	39	44.0	F.T.L.
59	39	B	4-0-0-5	38	43.2	F.T.L.
17	42	B	10-0-0-10	40	40.0	F.T.L.

was obtained for analysis, "ferric chloride number" (F.N.), and the outcome of the pregnancy (F.T.L., full-term living baby; L, premature baby who survived the neonatal period; and D, premature baby who was stillborn, or born alive but did not survive the neonatal period). Tables IV and V are summaries of the data shown in Tables I to III.

TABLE III. TWENTY CASES OF PREECLAMPSIA

CASE NO.	AGE	COLOR	PARITY	DURATION OF PREG. WHEN URINE OBT.	F.N.	BABY
5	27	W	0-0-0-0	38	45.5	F.T.L.
36	18	B	0-0-0-0	40	44.5	F.T.L.
40	16	B	0-0-0-0	39	42.0	F.T.L.
35	29	W	0-0-0-0	37	40.5	37D
60	14	B	0-0-0-0	34	40.0	F.T.L.
23	23	W	0-0-0-0	38	39.0	F.T.L.
63	21	W	0-0-0-0	40	38.5	F.T.L.
45	60	B	0-0-0-0	40	38.5	F.T.L.
37	28	B	0-0-0-0	40	38.0	F.T.L.
49	21	B	0-0-0-0	39	37.5	F.T.L.
66	19	W	0-0-0-0	40	37.2	F.T.L.
61	16	W	0-0-0-0	36	36.5	F.T.L.
10	19	W	0-0-0-0	40	35.5	F.T.L.
9	21	B	1-0-0-0	40	35.0	F.T.L.
64	24	W	0-0-0-0	40	34.5	F.T.L.
57	14	W	0-0-0-0	40	33.4	F.T.L.
48	21	B	0-0-0-0	32	32.0	F.T.L.
65	18	B	0-0-0-0	38	31.0	F.T.L.
22	17	B	0-0-0-0	34	30.0	34D
24	16	B	0-0-0-0	38	28.5	F.T.L.

TABLE IV. SUMMARY—TABLES I, II, III

	AVERAGE F.N.	F.N. RANGE	TOTAL NO. OF CASES	AVERAGE DURA- TION OF PREGNANCY, WEEKS
Normal	83.30	152.00-56.60	21	36.0
Chronic nephritis compli- cating pregnancy	51.67	64.00-40.00	19	37.1
Preeclampsia	36.87	45.00-28.50	20	38.1

In Tables I to III the parity of the patient is expressed in 4 figures according to a compact scheme, the origin of which is not known. The first figure represents the number of full-term children the patient has borne whether born alive or stillborn; the second figure gives the number of premature babies the patient has borne whether born alive or stillborn; the third figure indicates the number of abortions (termination of pregnancy on or before the twenty-eighth week); while the fourth figure shows the number of living children the patient has. In designating the parity of these patients by this method, the present pregnancy which has been studied has not been included, thus a primigravida is shown as a para 0-0-0-0.

## NORMAL CASES

The 21 cases shown in Table I were all normal in the sense that they were not suffering from any of the late toxemias of pregnancy which could be discovered clinically, and were admitted to the hospital mainly for convenience near term for the induction of labor. Seven were admitted because of the following complications:

Ischiorectal abscess  
Thrombophlebitis  
Pulmonary tuberculosis  
Rheumatic heart disease  
Cephalopelvic disproportion, 2 cases  
Salpingitis

Six of these patients were primigravidas and 15 were multigravidas; 13 were white and 8 were colored.

The average duration of pregnancy at the time the twenty-four-hour specimens were obtained was thirty-six weeks. The average "ferric chloride number" (F.N.) was 83.3, the highest being 152.0 and the lowest 56.6 (Table IV). Such a wide variation in this finding cannot be explained on the basis of the duration of pregnancy because with the exception of Case 54 (Table I) in which the duration of pregnancy was twenty-two weeks, the patients were from twenty-eight to forty weeks pregnant. Possible explanations of this wide variation are: first, individual variations in the amount of estrin excreted; and second, certain of these normal patients might have been on the verge of some toxemia which had not manifested itself clinically, but was accompanied by a lowered estrin excretion. This second idea is in keeping with the findings of Smith and Smith<sup>9, 10</sup> who observed that several of their patients did not develop clinical symptoms of toxemia until some time after a decrease in urinary estrin was noted. This, of course, suggests the possible prognostic value of periodic determinations of estrin excretion throughout pregnancy. Such routine determinations for all the patients registered in the prenatal clinic would not be possible at present.

All patients in the normal series were delivered of full-term living children who survived the neonatal period.

## CHRONIC NEPHRITIS COMPLICATING PREGNANCY

Table II represents a series of 19 cases of chronic nephritis complicating pregnancy, characterized by nitrogen retention in the blood, edema, albuminuria, and elevated blood pressure which failed to return to normal levels after delivery. One patient (Case 47, Table II) died following the interruption of her pregnancy because of severe chronic nephritis. This was the only maternal death in 60 cases or 1.6 per cent. All these patients were admitted to the hospital because of evidences of toxemia. There is but one primigravida in this series which is in keeping with the observation that chronic nephritis complicating pregnancy affects multigravidas more frequently than primigravidas. Many of these patients had symptoms of toxicity for from two to six months prior to delivery. Nine patients were white and 10 were colored.

The average duration of pregnancy at the time of collection of the twenty-four-hour urine was 37.1 weeks, while the average "ferric chloride number" (F.N.) was 51.67, the highest, 64.0, and the lowest, 40.0 (Table IV). The wide variation seen in the normal group was not found in this group.

In this series there were 13 full-term living children, a thirty-six-week stillborn baby, two each of thirty-six- and thirty-seven-week babies who survived the neonatal period, and one thirty-two-week living baby who survived the neonatal period.



These results also agree with the conception that premature babies are common in chronic nephritis complicating pregnancy.

No attempt was made to subdivide these patients into those who had suffered from chronic nephritis prior to the first pregnancy, or those developing chronic nephritis during the course of subsequent repeated pregnancies, or to differentiate between the types of chronic nephritis.

Smith and Smith<sup>9, 10</sup> obtained normal estrin levels in several patients who were definitely "nephritic." Our experience, on the other hand, has shown definite lowering of the level of estrin excretion in cases of chronic nephritis complicating pregnancy.

While chronic nephritis complicating pregnancy is not generally considered a true toxemia, we feel that the significant lowering of estrin excretion as found in our series of cases is worthy of mention, since it apparently has not been recorded elsewhere.

#### PREECLAMPSIA

The 20 cases of preeclampsia are shown in Table III. They were characterized by sudden elevation of blood pressure, sudden appearance of albumin in urine previously normal, increased uric acid retention in the blood, and by the sudden onset of subjective symptoms in late pregnancy varying from edema of the feet and ankles to edema of the face and hands, abnormal weight gain, nausea and vomiting, headache, precordial pain, and visual disturbances. All these patients were admitted

TABLE V. SHOWING EXCURSION AND OVERLAPPING OF F.N. IN THE THREE GROUPS OF CASES SUMMARIZED IN TABLES I TO III

F.N.		
152.0		
↓		
76.0		
67.6		
66.0		Normal group
66.0		
64.4		
64.0	64.0	
60.0	60.0	
59.2	59.5	
57.6	57.2	
56.6	56.0	
	55.0	
	54.5	
	52.5	
	52.4	Chronic nephritis com-
	52.0	plicating pregnancy
	51.0	
	51.0	
	49.0	
	48.5	
	48.0	
45.5	44.0	
44.5	44.0	
42.0	43.2	
40.5	40.0	
40.0		
39.0		
38.5		
38.5		Preeclampsia
38.0		
↑		
28.5		

to the hospital because of toxemia. In keeping with the observation that primigravidas are more prone to preeclampsia, we see that all but one patient in this series fall into this classification. Nine patients were white, 11 were colored. The average duration of pregnancy when the twenty-four-hour urine specimens were obtained was 38.1 weeks, while the average "ferrie chloride number" (F.N.) was 36.87, the highest 45.5, and the lowest, 28.5 (Table IV).

The pregnancies of the patients in this group terminated in the births of full-term living infants, with the exception of thirty-four-week and thirty-seven-week living premature babies who died in the neonatal period.

In this series we have confirmed the work of Smith and Smith<sup>8-11</sup> in finding a definitely lowered level of estrin excretion in preeclampsia (see Tables IV and V).

In Table V the excursion and overlapping of estrin excretion in the three groups of cases are given. In 18 cases, or 30 per cent, there is overlapping, but in 42, or 70 per cent, of the cases the results seem to be of value in differential diagnosis. Given "ferrie chloride numbers" of 83.3, 51.67 and 36.87 (Table IV), perhaps we would be justified in classifying the respective patients as normal, those suffering from chronic nephritis complicating pregnancy, and preeclamptic.

#### SUMMARY

1. By means of a chemical test for pregnancy<sup>6</sup> a definitely lowered level of estrin excretion in the urine has been found in a series of cases in the late toxemias of pregnancy. Determinations upon the urines of normal patients in the last trimester of pregnancy were run concurrently as controls to establish a normal level.

2. In this series preeclampsia was not subdivided into "low reserve kidney" and preeclampsia. The late toxemias of pregnancy are considered in this paper as: chronic nephritis complicating pregnancy, preeclampsia, and eclampsia. No cases of true eclampsia appear in this series.

3. Sixty hospitalized patients in the last trimester of their pregnancies were carefully studied clinically, and complete twenty-four-hour urine specimens were examined for estrin.

4. While the line of demarcation is not sharp in 30 per cent of the cases, it has been possible to divide 70 per cent into those normal patients who were free from any evidences of toxemia; those patients suffering from chronic nephritis complicating pregnancy; and those whose clinical diagnosis was preeclampsia. The average estrin excretion expressed as the "ferrie chloride number" for 21 normal cases was 83.30; for 19 cases of chronic nephritis complicating pregnancy, 51.67; and for 20 cases of preeclampsia, 36.87.

The authors wish to express their sincere appreciation to M. J. Schmulovitz for invaluable technical assistance and advice, and for his translations of some of the references; to Dr. L. H. Douglass for his review of this paper; and to the resident and nursing staffs of the Obstetrical Service in the University Hospital for their indispensable aid in obtaining the necessary specimens.

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LOMBARD AND GREENE STREETS

## THE BORDERLINE PELVIS

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ON SEVERAL occasions<sup>1</sup> I have made the bold inference that Smellie's theory of determining the length of the true conjugate diameter by subtracting 1.5 to 2 cm. from the diagonal, was not tenable. These statements had been based upon observation of occasional cases. In this communication I shall present facts and figures from my own systematic study of a series of cases, which are somewhat enlightening, especially in reference to what may be termed "the borderline pelvis." To my mind, "borderline pelvis" is as arbitrary a term as "test of labor." Textbooks give a specific definition, based upon the commonly practiced method of Smellie, the application of which frequently results in an inadequate test of labor and cesarean section, as well as an inaccurate understanding of the frequency and possibility of delivery through the natural route. The manner of handling the woman with a normal pelvis or the one with an absolutely contracted pelvis gives us little concern, and in such cases obstetric opinion does not vary. The class that falls in between these two limits requires the best obstetric judgment; and it is here that opinions vary.

My own conception of a borderline pelvis is one in which, disregarding a rigid perineum, the sacral promontory may be readily reached. This method eliminates the necessity of placing borderline pelvises into various groups with stated indications for treatment of each group. For I shall attempt to show that heretofore the vast majority of these cases have been improperly classified and subjected to the danger of radical procedures. In this paper I am concerned with the size of the pelvic inlet and not with classical means of grouping pelvises such as the excellent one proposed by Caldwell, Moloy, and D'Esopo.<sup>2</sup> It is pleasing to note that Fitzgibbon<sup>3</sup> does not consider it possible to classify contracted pelvises so as to lay down the treatment of cases in groups. Although he believes that the degree of contraction greatly influences the prognosis of the case, it does not exclude pelvic delivery in the major degrees, nor assure pelvic delivery in the minor degrees. Peckham and Kuder<sup>4</sup> in discussing labor in contracted pelvises wisely avoid confusion by regarding

a pelvis as contracted if the diagonal conjugate measures 11.5 cm. or less. Maxwell<sup>2</sup> selects the length of the diagonal conjugate rather than the estimated true conjugate as the determining measure, because the former is an actual measurement. Thus, modern authors are beginning to realize that little dependence may be placed upon the method of *estimating* the length of the true conjugate from the diagonal.

Patients with pelvises of normal contour, in whom the sacral promontory could be reached without difficulty, were selected from the prenatal clinics of Georgetown University, Garfield Memorial, Gallinger Municipal, and Columbia Hospitals. Although hundreds of patients had been examined, a complete study of the bony pelvis in a definite routine manner was made in eighty women. All measurements were

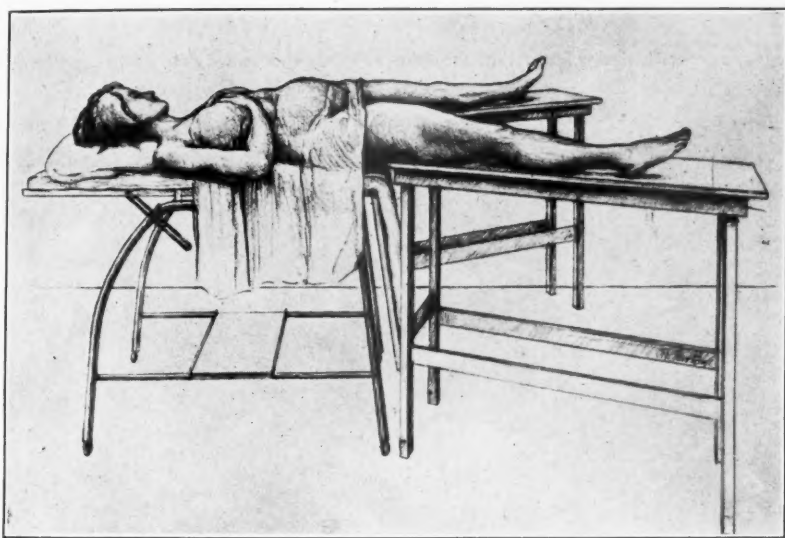


Fig. 1.—Patient recumbent for internal pelvimetry and anteroposterior roentgenography. Examiner stands between tables.

made with the obstetric inclinometer and it was necessary to select patients who would cooperate and lie perfectly quiet, for in using this instrument the pelvis must remain in a fixed position until all the necessary readings are taken. The patient is placed in the recumbent posture with legs extended and separated, being supported on two tables (Fig. 1). It is difficult to examine in this position, and unusual cooperation is required on the part of the patient. Yet it was necessitated by the fact that x-ray studies were made in the majority of these cases to confirm the calculations of the conjugata vera. Since variation in posture causes alteration in length of the true conjugate, it was necessary to examine patients in the same attitude (recumbent posture) in which they were placed for roentgenographic pelvimetry, thus en-

abling a check on all calculations. All examinations, calculations and roentgen interpretations were personally conducted, in order to eliminate, as far as possible, any source of error.

Williams<sup>6</sup> states: "Were we able to measure satisfactorily the angle formed between the symphysis and conjugata diagonalis, the exact length of the true conjugate could be ascertained." This is the procedure followed in the use of the inclinometer,<sup>1, 6</sup> where the height of the symphysis, the length of the diagonal conjugate and the size of the angle between them is noted. The calculator incorporated in the instrument enables accurate determination of the true conjugate diameter.

Reference has already been made to the fact that the inclinations of the symphysis and of the diagonal conjugate vary in all women.<sup>8</sup> Since it is these two angles that determine the size of the obstetric angle (which is that contained between the symphysis and diagonal

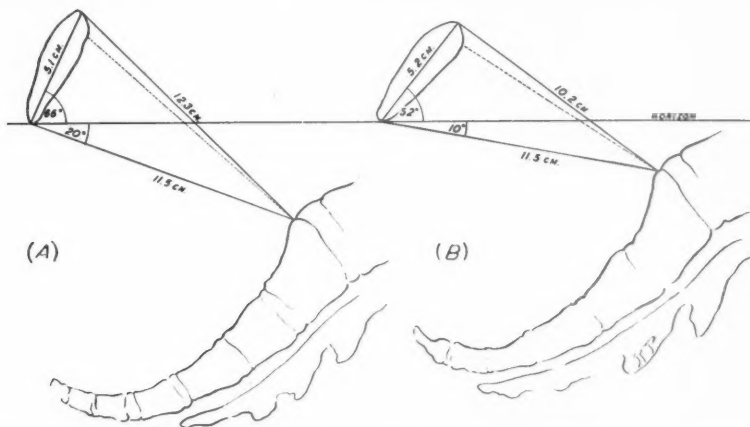


Fig. 2.—Two pelvis taken from the author's series. Although the diagonal conjugate diameters are equal, the true conjugate in (A) measures 12.3 cm. and in (B) 10.2 cm. Patient (a) delivered a 7 pound 14 ounce baby after a five-hour labor. Patient (b) was delivered of a 7 pound 7 ounce baby by cesarean section.

conjugate), it is readily understood that the size of the true conjugate cannot be determined by the length of the diagonal conjugate per se; and that seldom do we find two pelvis with identical diagonal conjugates in which the true conjugates are equal (Fig. 2). In all pelvis likewise, the inclination of the inlet varies, a factor that frequently is concerned with engagement regardless of pelvic dimensions.

It may be briefly stated that with a given diagonal conjugate a more favorable inclination of the symphysis causes a shortening of the true conjugate and vice versa (Fig. 2).

Since the factors that enter into the determination of the size of the true conjugate diameter are altered by changes in posture, postural changes warrant some consideration, as they may seriously affect the prognosis in a borderline pelvis. Although all textbooks make the statement that flexion of the thighs on the abdomen diminishes the true con-



jugate diameter and that hyperextension (as in Walcher position) causes increase in its length, no investigations had been conducted on living subjects to either prove or disprove these contentions, until those made by me a few years ago. Placing a patient in the lithotomy position causes shortening of the diagonal conjugate diameter, with increase in its inclination, a reduction in the inclination of the symphysis and a resulting shortening of the true conjugate diameter. The diminution in size of the true conjugate is usually between 0.5 and 1 cm., but

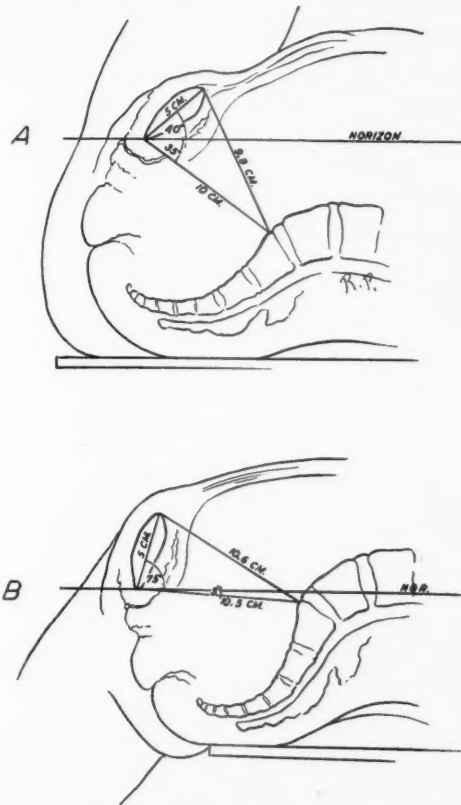


Fig. 3.—A, Patient in lithotomy position. B, Same patient in Walcher position. The factors responsible for alterations in length of pelvic diameters are shown. Note how, in the Walcher position, the tense abdominal muscles limit area over inlet and also prevent the rise of the fundus to its normal elevation at the height of a contraction; factors interfering with engagement.

varies in different subjects. In the Walcher position (Fig. 3), I have found an increase in the true conjugate, varying from 0.3 cm. to over 1 cm. This is effected by an increase in the length of the diagonal conjugate, and an increase in the angle of inclination of the symphysis; in this case, of course, inclination of the diagonal conjugate is diminished.

Since the Walcher position causes an increase in the conjugata vera and diagonalis, why has it not held a more popular place in the management of borderline cases? Possibly some obstetricians have doubted

whether it is possible to increase the size of the inlet by postural change, since observations of this type had never been made on living subjects. Although I have proof of the variation in size of the pelvic inlet, I have never advocated the use of the Walcher position. Besides being an uncomfortable attitude for a woman to assume during labor, the availability for engagement of the important pelvic planes is diminished. For when the thighs are allowed to hang over the edge of the table, an inlet that does not have a favorable inclination ordinarily becomes worse. The inclination of the symphysis likewise assumes a vertical attitude, making it necessary for a head to take a downward course in order to get beneath it, even if it succeeds in entering the brim. In addition the abdominal muscles are put under great tension and stretched over the in-

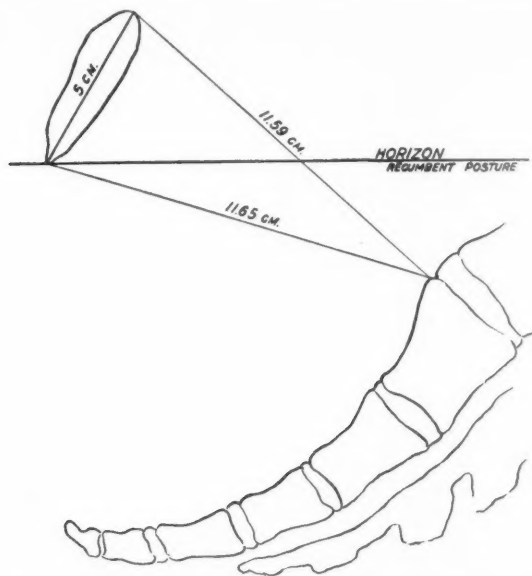


Fig. 4.—Pelvigram of the average pelvis in this series, with patient in recumbent posture. It will be recalled that in the ordinary modified lithotomy position in which women are usually measured, all diameters are somewhat smaller.

let, which is assuming a parallel position to the horizon, thus limiting the space over the inlet for engagement of the presenting part. Were the direction of the forces of expulsion correspondingly altered, so as to approach the axis of the superior strait, engagement would be facilitated. But what actually happens is a limitation of the motion of the uterus by the tense abdominal wall, so that the fundus cannot rise at the height of a contraction in an effort to bring the expulsive force in line with the axis of the superior strait, but is directed almost parallel with the inlet and more or less perpendicular to the symphysis. In a pelvis that has an unusually good inclination the Walcher position may not hinder engagement and be of some benefit by enlarging the inlet. In cases of moderately favorable or those of faulty inclination, the Walcher posi-

tion would be a disadvantage, for any increase in the size of the inlet is of no value, since the inclination of the plane of the inlet is such as to limit or even preclude its availability. It seems that the hanging leg position during labor may have a place only in borderline pelvis of unusually good inclination.

As previously stated, until recently the nearest approach to the measurement of the conjugata vera has been the deduction of 1.5 cm. to 2 cm. from the diagonal conjugate. With the aid of the inclinometer I have been able to *calculate* the length of the true conjugate with precision and check these determinations by both anteroposterior and lateral pelvimetric roentgenography and in some cases by direct measurement of the inlet at cesarean section. In the series of 80 cases the average diagonal conjugate was 11.65 cm. The average true conjugate was 11.59 cm. (Fig. 4). In 8 per cent of cases did the customary rule of subtracting 1.5 cm. to 2 cm. from the diagonal conjugate to obtain the true conjugate apply. In 89.5 per cent of the cases the difference was less than 1.5 cm. In 48.7 per cent of cases the true conjugate was either as large or larger than the diagonal conjugate. As judged by the length of the diagonal conjugate and the ability to feel the sacral promontory, my series represents a class of moderately contracted pelvis. Yet within this group we find a preponderance of true conjugate diameters that measure more than 11 cm. Note the large proportion of cases in which there is a small variation in the length of these two diameters. The true conjugate exceeded the diagonal in 37 cases; the size of the *obstetric angle*, which heretofore had been unmeasured, accounts for this.

TABLE I. ANALYSIS OF EIGHTY BORDERLINE PELVES IN RECUMBENT POSTURE, SHOWING ACTUAL CALCULATED TRUE CONJUGATE DIAMETERS AND METHODS OF TREATMENT

TRUE CONJUGATES	NORMAL DELIVERY	LOW FORCEPS	MID- FORCEPS	CESAREAN SECTION (ALL FOR DISPRO- PORTION)	TOTAL
13 to 12 cm.	19	6	0	1	26
11.9 to 11 cm.	27	4	1	1	33
10.9 to 10 cm.	10	0	1	6	17
9.9 to 9 cm.	3	0	0	1	4
8.9 to 8 cm.	0	0	0	0	0
Total	59	10	2	9	80

In this series 59 patients had true conjugates of over 11 cm.; yet I have reason to consider them borderline cases, for if measured in the modified lithotomy position the diagonal conjugates would be 11.5 cm. or less. In this class there were 46 normal deliveries, 10 low forceps, 1 midforceps, and 2 cesarean sections. Between 10 and 10.9 cm., 6 cesarean sections were done in 17 cases; there was one maternal death due to infection following section. This patient, in my opinion, did not

receive a sufficient test of labor; abdominal operation could have been avoided, but that operator believes in a six-hour test of labor. There were no cases of true conjugate actually measuring less than 9 cm. in this series, showing that such pelvises are extremely rare. These figures are consistent with the views of Fitzgibbon<sup>3</sup> who states that 70 to 80 per cent of patients with borderline pelvises deliver normally.

The smallest pelvis that permitted delivery of the largest baby (9 pounds 6 ounces) from below, was one with a calculated true conjugate of 9.1 cm. or an available true conjugate of about 8.5 cm. Labor lasted fifteen hours. The largest pelvis that required cesarean section after a suitable test of labor had an available true conjugate of 11 cm., the baby weighing 9 pounds 2½ ounces. Such occurrences, although uncommon, are in accord with the view of Fitzgibbon<sup>3</sup> who stated that the amount of contraction does not always exclude pelvic delivery even in the major degrees, nor assure pelvic delivery in the minor degrees.

I naturally conclude that in the average patient the true conjugate diameter measures more than 11 cm. and that the difference between the true and the diagonal conjugate is less than 1.5 cm. This fact should persuade us to be more generous with the test of labor. It emphasizes also that one is not justified in placing a pelvis in the borderline or contracted group, merely because of a true conjugate diameter that has been estimated from the diagonal conjugate by the usual means advocated by Smellie. Most women with borderline pelvises deliver through the natural channel and usually spontaneously, because the true conjugate is actually larger than we have been accustomed to estimate.

TABLE II. ACCORDING TO SMELLIE'S METHOD, THE SAME SERIES OF PATIENTS, IF EXAMINED IN MODIFIED LITHOTOMY POSITION, WOULD BE IMPROPERLY GROUPED

TRUE CONJUGATES	NORMAL DELIVERY	LOW FORCEPS	MID- FORCEPS	CESAREAN SECTION (ALL FOR DISPRO- PORTION)	TOTAL
11.5 to 10.5 cm.	8	0	0	0	8
10.4 to 9.5 cm.	30	7	0	4	41
9.4 to 8.5 cm.	20	2	2	3	27
8.4 to 7.5 cm.	2	0	0	2	4
Total	60	9	2	9	80

By Smellie's method in the usual modified lithotomy position, there would be no patients with a true conjugate over 11.5 cm., and this has been the general concept. Forty-one patients would be classed as having a true conjugate of 10.4 to 9.5 cm., and of these 4 had cesarean sections and 7 low forceps. Twenty-seven patients would be regarded as having a true conjugate of between 8.5 and 9.4 cm., and as such would probably have received a very short and inadequate test of labor, and more than 3 cesarean sections might have been performed in this group. All 4 patients with a true conjugate between 7.5 and 8.4 cm., under

ordinary circumstances might have been sectioned, instead of just two.

The smallest pelvis that I have ever encountered was one that had a calculated true conjugate of 8 cm. (Fig. 5). I have never before or since seen one that actually measured less; and that covers examinations of several thousand women. According to Table II such pelvis are erroneously believed to be common; in this table there appears to be a frequency of 5 per cent.

Ample reason has been given why a diagnosis of borderline pelvis should not be made from true conjugates that are estimated from the diagonal by subtracting 1.5 cm. to 2 cm. This method in actual practice affords a distorted prognosis, in view of the figures presented. Williams<sup>5</sup> like most authorities regards a pelvis with an estimated conju-



Fig. 5.—A-P roentgenogram of smallest pelvis encountered in the various clinics, showing that pelvis customarily classified as absolutely contracted are extremely rare. (The middle of the upper border of the symphysis is designated by the heavy line.)

gata vera of 9 to 10 cm. as being in the mild borderline class and says that spontaneous delivery with a full-term baby of normal size and with normal expulsive forces is the rule. In this class he refers to pelvis with a diagonal conjugate varying between 12 and 10.5 cm. The vast majority of these should and do deliver normally, because the true conjugate in 89 per cent of them is much larger than 9 to 10 cm. And in borderline pelvis of the more severe type, that is, presumed to be between 9 and 7.5 cm. and estimated from diagonal conjugates varying between 10.5 and 9 cm., he says the greatest difficulty is experienced in predicting the course of labor and in laying down rules of treatment. I feel that in cases in this type, since the true conjugate frequently equals or may surpass the length of the diagonal conjugate, some patients should stand



a chance of delivering from below, especially where the fetal skull is not large and the diagonal conjugate is nearer to 10.5 cm.

With a true conjugate diameter of 9 cm. as calculated with the inclinometer, experience shows that a full-term baby of average weight will very seldom deliver spontaneously, for reduction in the size of the biparietal diameter may be limited. Where the true conjugate diameter really measures 8.5 cm. or 8 cm. or less, delivery of a living full-term child through the birth canal is hardly possible. For we must further deduct from such a diameter 0.7 cm. to reduce the true conjugate diameter to the obstetric, or better term is the available conjugate.

In my series there were two fetal deaths. Both fetuses died of intracranial hemorrhage; one weighing 6 pounds 14 ounces followed Scanlon maneuver in a pelvis with an available conjugate of 10.7 cm.; the other followed normal delivery in a pelvis having an available conjugate of 12 cm.

Regarding the prognosis for the fetus in borderline and contracted pelvises, Williams<sup>6</sup> quotes as examples figures from Michaelis, Litzmann and Schwartz, giving the mortality prior to 1865, when cesarean sections were seldom performed.

CONJUGATA VERA	FETAL MORTALITY
1. 9.25 to 8.5 cm.	5%
2. 8.4 to 7.5 cm.	16.9%
3. 7.4 to 7.0 cm.	52.9%

From my study it may be safely assumed that these rates are too exceedingly low to be correct, and may be accounted for by reference to my remarks, that the conjugata vera in these cases had been estimated from the diagonal. That in reality direct mensuration, had it been possible, would have revealed pelvises much larger than stated in the above table. It should be recalled that from the above tabulated measurements, 0.7 cm. must be deducted to obtain the "available true conjugate." Therefore I disagree entirely, and safely conclude that for pelvises as stated in Class 1 the fetal mortality is and should be much greater. In Class 2, engagement of a normal size head is almost always impossible. In Class 3, engagement of a normal size head is always impossible.

These statements are not made to encourage the performance of cesarean section, but, on the contrary, to call to the attention of the obstetrician the fact that he often is dealing with a larger pelvis than he surmises, and that in borderline cases there is usually a good chance of his patient delivering from below. It may be said without hesitation that pelvises actually measuring 8.5 cm. or less in the true conjugate are not ample for safe delivery of a child of normal size. I should call these absolutely contracted pelvises. Then the lower limit of borderline pelvises would be about 9 cm. for the true conjugate, or 8.3 cm. for the available conjugate, for we deduct 0.7 cm. as being the

distance from the middle of the thickness of the pubic symphysis to the posterior surface. Therefore, were it possible to classify contracted pelvises by direct measurement of the conjugata vera, we would find that most pelvises that are now placed in the borderline class would permit spontaneous delivery, for they are larger than estimated. We would be surprised to find that the average pelvis is larger than we believe it to be. Also the upper limit of the absolutely contracted class should be raised, so as to include larger true conjugates. Pelvises of the absolutely contracted type as determined by Smellie's method (that is, with a true conjugate of 7.5 cm. or less) are very uncommon.

#### SUMMARY

In the series presented there were 59 normal deliveries, 10 low forceps, 2 midforceps and 9 cesarean sections. The one maternal death could have been avoided, for it resulted from cesarean section following inadequate test of labor. Only 2 infants were lost; both deaths were due to intracranial hemorrhage.

#### CONCLUSIONS

1. Definite rules concerning the formerly accepted classifications and treatment of contracted pelvises are not tenable.
2. When the sacral promontory is readily palpated, the pelvis should be classed as borderline.
3. In the series presented, all measurements were made in the recumbent posture; if examined in the usual modified lithotomy position, the internal measurements of these pelvises would have been somewhat smaller.
4. The outcome in a borderline pelvis is not only governed by size of the "available true conjugate diameter," but also by the inclination of the inlet.
5. The value of the Walcher position is not strongly endorsed.
6. Proper recognition of borderline pelvises from the length of diagonal conjugates with disregard to Smellie's rule of subtracting 1.5 to 2 cm., will result in better tests of labor and fewer cesarean sections. In only 8 per cent of cases does Smellie's rule apply.
7. The mere application of Leopold's fourth maneuver is of greater prognostic value in borderline cases than grouping pelvises according to true conjugates which were estimated by Smellie's method.

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WASHINGTON MEDICAL BUILDING

## EXTRAPERITONEAL (LATZKO) CESAREAN SECTION\*

WITH A REPORT OF CASES AND SUGGESTED MODIFICATIONS IN TECHNIC

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*(From the Clinic of the Woman's Hospital)*

ACCUMULATED experience with the extraperitoneal (Latzko) cesarean section, in various obstetric clinics throughout the country, is gradually serving to establish it as an invaluable means of delivery for selected cases.

The purposes of this paper are:

1. To discuss the indications for extraperitoneal cesarean section and to emphasize its advantages as a means of delivery when indicated.
2. To describe a point in technic which during dissection should reduce the danger of bladder injury.
3. To present a modification in technic whereby the Latzko procedure is made adaptable for the suprapubic delivery of a patient regardless of whether or not the cervix is dilated and retracted.
4. To demonstrate a method for more adequate drainage of the space of Retzius following delivery by the Latzko procedure.
5. To report a small series of patients delivered by this method at the Woman's Hospital.

It is my opinion that indications for extraperitoneal cesarean section arise in two classes of infected or potentially infected cases as follows:

1. Cases in which, through faulty judgment, it is eventually found in the course of labor that, because of bony dystocia, vaginal delivery of a living child is impossible or extremely problematical. Delivery by extraperitoneal cesarean section has been successfully accomplished in such cases after attempted operative delivery by vagina.
2. Cases in which, in spite of prolonged first-stage labor, the cervix has failed to dilate. This group of cases includes those which have true cervical dystocia and those in which the cervix has failed to dilate as the result of primary uterine inertia.

When, in the best interests of the mother or child, delivery of such patients becomes necessary, we are frequently faced with possible uterine infection which has been favored by early rupture of membranes, the contamination of repeated vaginal examinations and a mother whose vitality and resistance have been reduced by the conditions resulting from prolonged first-stage labor. Such patients also frequently have borderline pelvises, usually of the male type, and large babies showing signs of fetal distress.

\*Read at a meeting of the New York Obstetrical Society, October 13, 1936.

Experienced obstetricians are familiar with the difficulties and dangers which attend vaginal delivery, before full cervical dilatation has been reached. As a rule, it involves:

1. Manual dilatation of the cervix or multiple (Dührssen's) incisions.
2. A difficult operative delivery which occasionally either necessarily sacrifices the life of the infant or leaves the infant with some degree of physical handicap, the result of birth injury.
3. An immediate risk to the mother from trauma, hemorrhage, shock, and infection, and finally the possibility of some degree of permanent physical handicap from unavoidable vaginal or uterine birth injuries, which may be difficult to repair.

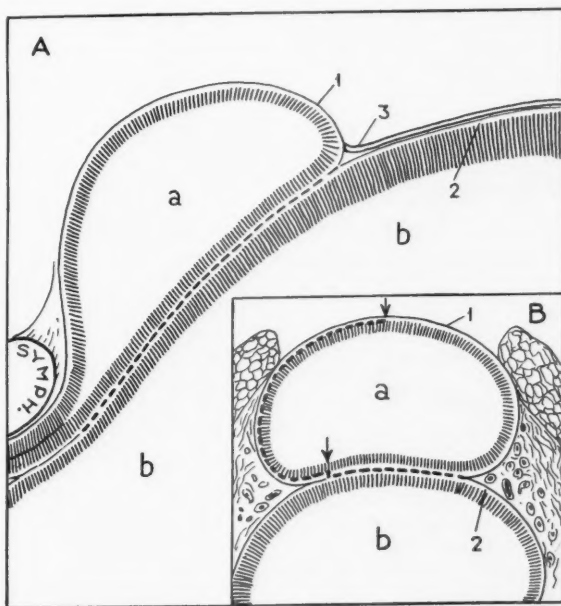


Fig. 1.—Diagram showing anatomic relationships of bladder and anterior uterine wall in A, the sagittal plane and in B, cross-section. *a*, Bladder. *b*, Uterine cavity. 1, Endopelvic fascia completely surrounding the bladder musculature. 2, Endopelvic fascia surrounding the musculature of the uterus. 3, Uterovesical fold or peritoneum. The dotted line, between the layers of endopelvic fascia covering the bladder and lower uterine segment, shows the proper plane of cleavage in which dissection can be readily and safely carried out. It is the space which is opened in the so-called "low flap" cesarean section. In B, the arrows indicate the points at which the endopelvic fascia about the bladder is opened during the dissection. It will be noted that as soon as the anterior uterine segment is reached, the endopelvic fascia on the posterior surface of the bladder is opened and dissection is continued between this layer and a similar layer on the uterine musculature.

Those interested in an historical review of the technical development of extraperitoneal cesarean section and a complete description of the details of the Latzko technic are referred to articles by DeLee,<sup>1</sup> Steele,<sup>2</sup> and Burns.<sup>3</sup> It is the purpose of this paper to suggest three additional points in technic, not previously described, which it is believed, in certain cases, may facilitate the performance of the procedure and contribute to its safety.

One of the greatest objections to the Latzko operation has been the danger of bladder injury, during dissection, to expose the anterior surface of the lower uterine segment. In Steele's<sup>2</sup> series of 59 cases this accident occurred six times. In our own series of 27 cases the bladder was accidentally opened once.

A study of the anatomic structures around the bladder (Fig. 1, *A*) shows that its musculature is completely surrounded by a thin but definite layer of endo-

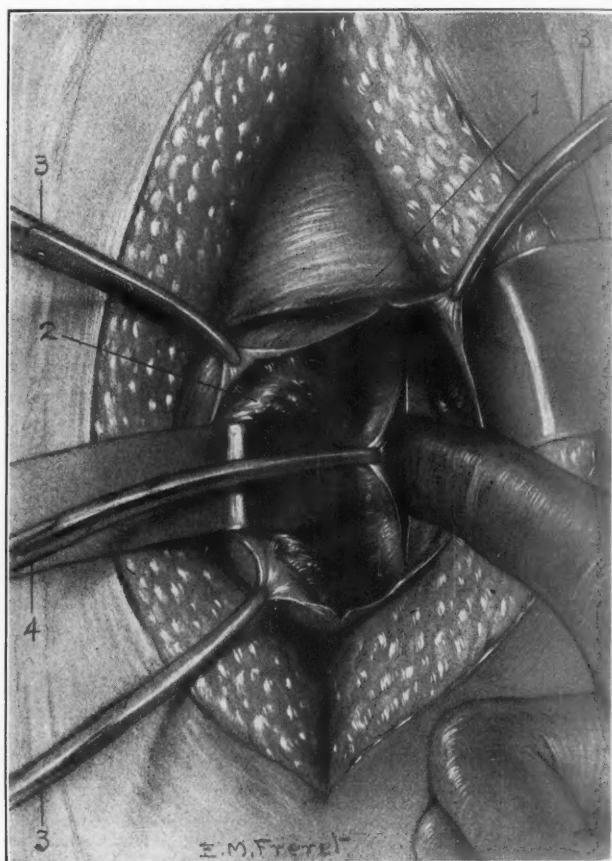


Fig. 2.—Diagram showing bladder displaced laterally and endopelvic fascial capsule about bladder. 1, Uterovesical fold of peritoneum. 2, Bladder. 3, Clamps on incised endopelvic fascia on anterior surface of bladder. 4, Clamps on incised endopelvic fascia on posterior surface of bladder. Blunt dissection is continued behind this layer rather than within the endopelvic fascial capsule of the bladder.

pelvic fascia (Fig. 1, *A*, 1). After incising the abdominal wall the first step in dissection is to open the layer of endopelvic fascia (1), covering the anterior surface of the distended bladder by a longitudinal incision in the midline. After this layer has been incised, the bladder can easily be displaced, from within its endopelvic fascial capsule<sup>1</sup> on the left side (*B*), by blunt dissection. As soon as the anterior surface of the lower uterine segment is reached (Fig. 1, *B* and Fig. 2), the layer of endopelvic fascia on the posterior surface of the bladder can readily be seen as a



smooth glistening layer. It has been found that this layer can be immediately opened and dissection can more readily be continued behind the layer (Fig. 1, *B* and Fig. 2), rather than making further attempt to free the bladder from its fascial capsule. When dissection is continued between this layer (Fig. 1, *B*, 1), and a similar layer (Fig. 1, *B*, 2) covering the musculature of the lower uterine segment, it will be found that a free, practically bloodless, space has been entered and that the anterior surface of the lower uterine segment can readily be exposed. Between these fascial planes (Fig. 1, 1 and 2) the dissection can easily be carried laterally or upward behind the uterovesical fold of peritoneum (Fig. 1, 3), far beyond the upper border of the bladder. This is exactly the same almost bloodless space which is entered in displacing the bladder downward in doing the so-called "low flap" cesarean section by the abdominal route.

It is believed that bladder injury usually occurs when, in order to get adequate exposure of the lower uterine segment, persistent efforts are made to continue the dissection posteriorly within its fascial capsule.

Another serious criticism of the Latzko operation has been the fact that the uterovesical fold of peritoneum is too frequently opened during the operative dissection or while extracting the infant. If the injury occurs before the uterine cavity is opened, it can be immediately repaired to prevent later contamination of the peritoneal cavity. However, if the peritoneal cavity is accidentally opened during extraction of the infant, contamination of the peritoneum is bound to occur, thereby defeating the purpose of the procedure.

Previous writers on this subject have invariably claimed that the procedure, as a means of suprapubic delivery, is inadvisable unless the cervix is at or near full dilatation. The advantages are that when cervical dilatation is well advanced, and the cervix is at least partially retracted, the lower uterine segment increases in length; the uterovesical fold of peritoneum is elevated, and the uterine vessels and ureters are laterally displaced. These physiologic changes in relationship of the structures, for obvious reasons, greatly facilitate the procedure.

In our experience, indications for extraperitoneal cesarean section occasionally arise in obese women with male pelves and large babies, in whom adequate exposure of the lower uterine segment is difficult, even though these changes have occurred. Furthermore, in our experience the most frequent indication for extraperitoneal section occurs in women in whom, in spite of prolonged first-stage labor, the cervix has failed to dilate more than 3 to 5 cm., because of true cervical dystocia, or uterine inertia or both. In spite of careful dissection, in either of these types of cases, it is frequently impossible to get sufficient exposure of the lower uterine segment in order to deliver the infant without considerable danger of opening the uterovesical fold of peritoneum. When the available space is obviously too limited to deliver the infant, without danger of peritoneal injury, we have recently deliberately incised the uterovesical fold, on the left side, as shown in Fig. 3. By this means free exposure of the lower uterine segment can be readily obtained regardless of how much the cervix is dilated or retracted. The free margins of

the peritoneum are carefully brought into apposition, as shown in Fig. 4, before the uterine cavity is opened. This procedure not only gives room for delivery in cases where it is difficult or impossible to get adequate exposure of the lower uterine segment, but makes the procedure available as a means of delivery regardless of the degree of cervical dilatation or retraction.

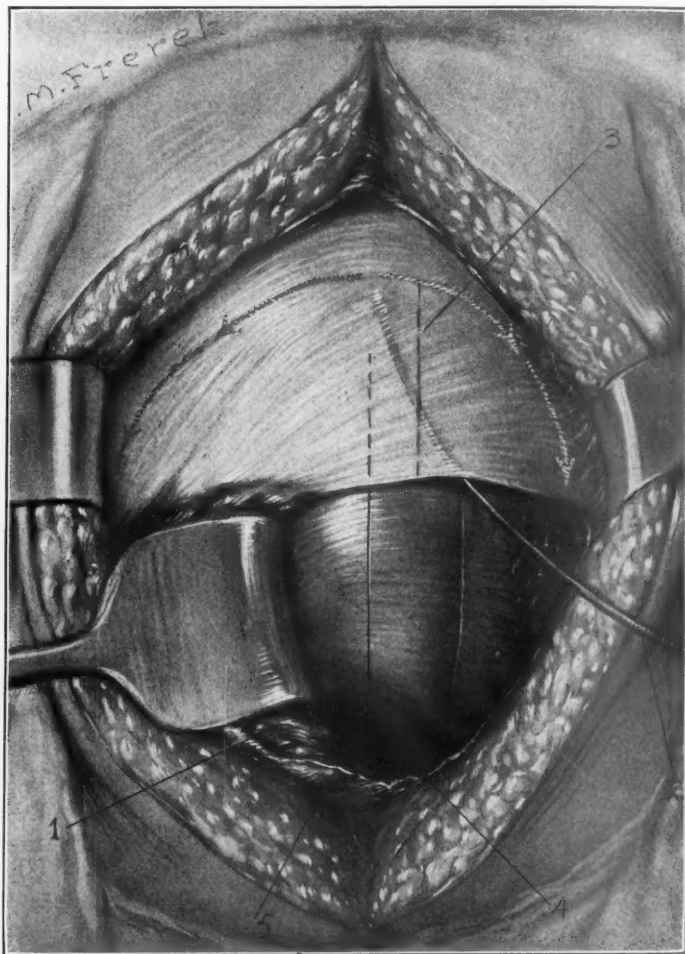


Fig. 3.—1, Retracted bladder. 2, Probe under dissected tense uterovesical fold of peritoneum. 3, Line of incision through uterovesical fold of peritoneum. 4, Line of incision in lower uterine segment.

It is admitted that deliberate opening of the peritoneal cavity, as described, is a violation of the principle of extraperitoneal cesarean section. However, the incised peritoneum can be securely closed by careful suturing so that subsequent contamination of the peritoneal cavity through the suture line must be slight, if any. This step in technic has been successfully used in four frankly infected cases.

One of the most important steps in the technic of extraperitoneal cesarean section, to insure safety of the procedure and to promote satisfactory wound healing, is the establishment of adequate drainage of the space of Retzius. In the past it has been customary to use, for this purpose, one cigaret drain, which was placed beside the bladder, and passed

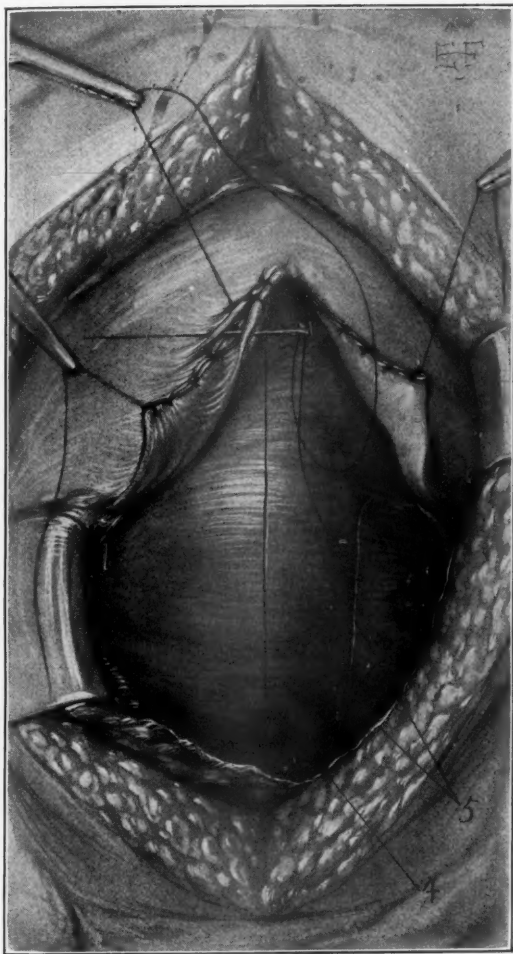


Fig. 4.—Method of closing incised uterovesical fold of peritoneum. 5, Incised edge of posterior layer of endopelvic fascial capsule of bladder.

out through the lower angle of the abdominal incision. This drain was removed after two to seven days and, in most cases, seemed adequate for the purpose. However, certain patients had profuse drainage and persistent troublesome drainage sinuses for some time after operation.

Recently, we have used, in addition to drainage through the lower angle of the abdominal incision, a second small cigaret drain as shown in Fig. 5. This drain is placed between the bladder and lower uterine

segment and is passed out through the lower angle of the uterine incision, where it is fixed in position, by one suture of No. 0 catgut. The lower end of this drain is allowed to protrude into the lower uterine segment and vagina for about four to five cm. At the end of five to seven days, it can be easily removed through the vagina. This step in technic allows dependent drainage of the space of Retzius. In the seven cases in which it has been used, there was a minimum of postoperative reaction and the abdominal wounds healed promptly.

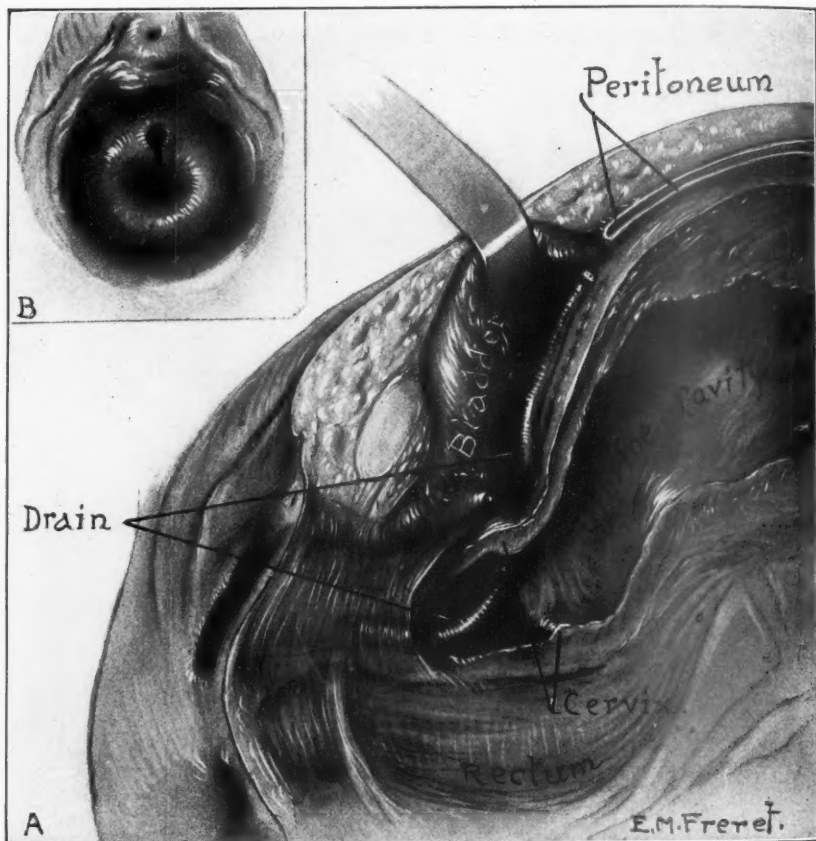


Fig. 5.—A, Diagram showing method of dependent drainage of space of Retzius, by drain passed through lower angle of uterine incision. Inset B shows observed drainage opening in anterior lip of cervix two weeks after operation.

Criticism of drainage through the lower uterine segment, possibly leaving a weak spot which might rupture during a future labor, is anticipated. In defense of this criticism, attention is called to the fact that the lower end of the uterine incision, used for the Latzko operation, always comes very close to the upper margin of the vagina. Inspection of the cervix following removal of this drain has shown it passing through the vaginal portion of the cervix as in inset "B," Fig. 5. Even

if the drainage opening persisted, which seems unlikely, it would weaken the wall no more than a deep cervical laceration. On the other hand nothing should insure good healing of the uterine incision, as a whole, so much as free postoperative drainage of the infected space between the bladder and lower uterine segment.

In the following six tables is recorded a summary of the data regarding 27 extraperitoneal (Latzko) operations done by eight members of the Woman's Hospital staff.

In Table I it will be noted that 22 of the 27 patients operated upon were at term with their first pregnancies; that two-thirds had contracted pelvis; that four had had previous complicated deliveries; and that five were toxic. Contracted pelvis, in this group of cases, were invariably borderline in type, justifying adequate trial labor.

TABLE I. SUMMARY OF DATA REGARDING LATZKO OPERATIONS PERFORMED FROM 1930 TO DATE

No. of patients	27
No. of operations	27
Elective operations	0
After trial labor	27
No. of operating surgeons	8
Average age of patients	29.4 years
History of pregnancies:	
Gravid i, 22; Para i, 2; Para ii, 2; Para iii, 1	
<i>Antepartum conditions</i>	
Type of pelvis:	
Normal	9
Justominor	9
Male or funnel	7
Simple flat	2
Toxemia	5
Previous complicated labors	4
Pyelitis	1
Congenital dislocation of hip	1

Table II is a summary of the progress of labor in the 27 patients at the time they were operated upon. It will be noted that the average duration of ruptured membranes was 40.7 hours; that the average duration of labor was 38.8 hours; and that in 21 of the 27 cases the head had failed to engage. More than two-thirds of the cases had some degree of uterine inertia. The average cervical dilatation was 4.3 cm. Considering these facts, there is little doubt that these cases should be looked upon as, at least potentially, infected at the time of operation.

TABLE II. SUMMARY OF FINDINGS, AFTER THE 27 TRIAL LABORS, AT TIME OF OPERATION

Onset: Spontaneous	24
Induced—Voorhees' bags—toxemia	2
Induced—rupture of membranes postmaturity	1
Type of labor: Good 8, fair 12, poor 7.	
Membranes: Intact 2, ruptured 25. Average	
duration of ruptured membranes (25 cases)	40.7 hr.
Average duration of labor	38.8 hr.
Presentation: breech 1, vertex 26.	
Level of presenting part: Engaged 6, unengaged 21.	
Average dilatation of cervix	4.3 cm.



Table III is a summary of operative indications. Two-thirds of the patients operated upon had contracted pelvis. In only one patient was the cervix fully dilated. In 26 of the 27 patients, the average cervical dilatation, at time of operation, was 4.8 cm. in spite of an average first-stage labor, in these cases, of 40.7 hours and an average duration of ruptured membranes of 38.8 hours. These patients had an average of four vaginal examinations before operation. Maternal exhaustion and evidence of fetal distress, in some cases, were factors influencing the decision to terminate labor. Two cases were successfully delivered of living children after attempted high forceps operations.

TABLE III. OPERATIVE INDICATIONS

Normal pelvis, good labor, cervical dystocia	3
Normal pelvis, inertia uteri, cervical dystocia	6
*Contracted pelvis, good labor, cervical dystocia	6
Contracted pelvis, inertia uteri (fully dilated)	1
Contracted pelvis, inertia uteri, cervical dystocia	11
	—
	27
<i>Other Conditions at Time of Operation</i>	
Maternal exhaustion	4
Fever and tachycardia	6
Respiratory infection—toxemia	1
Fetal distress	8
Unsuccessful high forceps	2

\*One operation done to protect premature (31 wk.) baby.

Table IV is a summary of data regarding anesthesia, duration of operations, wound drainage, and postoperative reactions. We can confirm the observations of other writers regarding the fact that, in spite of extensive dissection, a minimum of disturbance of bladder function accompanies the procedure.

The average weight of the babies delivered was 7 pounds, 9 ounces.

TABLE IV. SUMMARY OF THE 27 LATZKO OPERATIONS

Anesthesia: Gas-oxygen and ether, 26; gas-oxygen and spinal, 1	
Average duration of operations, 61 minutes.	
Drainage of space of Retzius:	
Abdominal	20
Abdominal and through uterine incision	7
Postoperative fever:	
Average duration	8.2 days
Average high point	102.3 degrees
Postoperative catheterization:	
None	8
Once to twice	13
Retention catheter for 48 to 72 hours	6
Weight of babies (3 pounds, 9 ounces to 10 pounds, 7 ounces):	
Average, 7 pounds, 9 ounces.	
Postoperative days in hospital:	
Average 18.1	

Table V shows the incidence of operative complications. In one case the bladder musculature was injured, while extracting the child, but the bladder itself was not opened. In another case, the finger of an assistant was accidentally pushed through the bladder wall while retracting the bladder manually. This accident

was probably favored by overdistention of the bladder with fluid to assist in making the dissection. The uterovesical fold of peritoneum was accidentally opened in five patients.

TABLE V. COMPLICATIONS OF OPERATIONS

Bladder injuries:	
Musculature only	1 case
Bladder opened	1 case
Peritoneal injuries:	
Uterovesical fold opened	5 cases
Uterovesical fold opened deliberately to get exposure	3 cases

Table VI is a summary of postoperative complications. The most frequent complication was faulty wound union. One patient died of coronary occlusion, the only serious postoperative complication which occurred. Considering the type and physical condition of patients operated upon, we feel that, on the whole, they had surprisingly uneventful recoveries.

There was one neonatal death of a premature baby from bronchopneumonia.

TABLE VI. POSTOPERATIVE COMPLICATIONS

Maternal:	
Faulty wound union—1 wound resutured	8
Shock, mild	5
Nausea and vomiting	4
Upper respiratory infection	3
Pyelitis	2
Sapremia	2
Coronary occlusion (death)	1
Pleurisy	1
Toxic psychosis	1
Dermatitis (iodoform)	1
Retained secundines	1
Fetal:	
Prematurity (31 wk.) bronchopneumonia death	1

Table VII is a brief summary of the follow-up of patients operated upon and of the one maternal and one neonatal death which occurred in the series. Three patients had subsequent pregnancies.

The one maternal death occurred suddenly, of coronary occlusion, ten days after operation. Until this accident manifested itself, the patient was apparently making a satisfactory recovery. Her temperature was normal on the day that symptoms of coronary occlusion appeared. At time of operation, the cervix was 5 cm. dilated, and the head of the baby, weighing 7 pounds, 12 ounces, was just engaged in a R. O. P. position. The pelvis was normal in size. The membranes ruptured at the onset of fifty-four hours of first-stage labor. During the last eighteen hours, the contractions were frequent and hard. At time of delivery, she showed signs of exhaustion. She had fever, a rapid pulse, and had had chills.

The one neonatal death occurred forty-eight hours after delivery, in a baby delivered at thirty-one weeks of pregnancy, weighing 3 pounds, 9 ounces. The mother had had a previous premature labor at twenty-four weeks' gestation and was extremely anxious for this child. She had had uterine bleeding on several occasions during her pregnancy and had spent much of the time in bed. For two weeks before delivery she had had scant bleeding off and on and painful

uterine contractions. At time of operation she had a foul vaginal discharge. Soon after labor finally started, at thirty-one weeks, the baby showed signs of distress, and suprapubic delivery was resorted to as a means of saving the baby. Autopsy showed that death was due to bilateral bronchopneumonia, probably the result of aspiration before delivery.

TABLE VII. FOLLOW-UP

All wounds healed at 6 weeks after operation
Subsequent pregnancies, 3
1 Delivered by low flap cesarean section
1 Delivered by prophylactic low forceps
1 At present in antepartum clinic
<i>Mortality</i>
Maternal: 1 death
Condition satisfactory until tenth postoperative day. Died suddenly of coronary occlusion.
Fetal: 1 neonatal death
Premature (31 wk.) baby died 48 hours after birth. Autopsy showed bronchopneumonia, bilateral

In a recent article entitled, "The Abuse of Caesarean Section,"<sup>24</sup> a plea has been made for obstetricians to reduce the number of deliveries by this method and, when indications arise, to resort to the older obstetric procedures, such as craniotomy, internal podalic version, forceps, cervical incisions, and dilatation of the cervix by use of hydrostatic bags.

The disadvantages and dangers of these methods are too familiar to members of this society to need any discussion.

From our limited experience with extraperitoneal cesarean section, we are doubtful as to whether craniotomy, especially in a living child, is ever necessary.

On account of the dangers and unsatisfactory results of attempting to complete cervical dilatation by the use of hydrostatic bags, we have practically abandoned this method of treatment.

The advisability of manually completing cervical dilatation or resorting to cervical incisions, in order to terminate labor, must be decided in the individual case. We are convinced that these procedures are definitely unsuitable for some of the patients in whom the cervix has failed to dilate after prolonged first-stage labor.

Internal podalic version, which is attended by a high rate of fetal mortality and a high incidence of maternal and fetal birth injuries, has been used as a method of delivery for nearly every known obstetric complication. Fortunately, for both mothers and their babies, the indications for this procedure have diminished as refinements in operative obstetric technic have developed.

Undoubtedly some of the cases in this series, if handled in other obstetric clinics, would have been delivered by low flap cesarean section. In none of the patients, when studied individually, could it be denied that there would have been a real danger of infection if delivered through the abdomen.

Success with the extraperitoneal (Latzko) cesarean section demands:

1. Obstetric skill and experience to select cases with proper indications for the procedure.
2. A thorough knowledge of the anatomic relationships about the bladder and lower uterine segment.
3. Training and experience in surgery as well as obstetrics, in order to apply successfully the procedure, and to avoid unnecessary surgical complications.

From our limited experience with the Latzko operation we are convinced that when proper indications arise:

1. It is an invaluable procedure for the suprapubic delivery of infected or potentially infected cases.
2. The method of approach, for extraperitoneal cesarean section, offered by the Latzko technic, is anatomically the most logical one yet developed.
3. The technic of the procedure is safe and not too difficult for those well trained in gynecology as well as obstetrics.
4. Bladder injuries can be prevented by a knowledge of the endopelvic fascia and dissection in the proper planes of cleavage.
5. In order to get adequate exposure of the lower uterine segment, and to prevent accidental injury to the peritoneum and contamination of the peritoneal cavity, it may be wise in certain cases, to incise the utero-vesical fold of peritoneum deliberately, by the method described, before the uterine cavity is opened.
6. Dependent drainage of the space of Retzius will promote healing of the uterine and abdominal incisions and increase the safety of the procedure.
7. Maternal mortality, from cesarean section, could be reduced, if obstetricians would familiarize themselves with the technic of the extraperitoneal operation, and refuse to adopt the abdominal route in cases where preoperative conditions, known to favor uterine infection, have existed.

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#### DISCUSSION

DR. KYLE B. STEELE.—Some time ago, in performing a Latzko section, I found that the space which could be exposed in the lower uterine segment was entirely inadequate. On the spur of the moment, I resorted to a Y-shaped incision, the limbs of the Y being placed below the peritoneal reflection. I found that this move provided adequate room. I have tried this modification since that time, and feel that it is a very valuable procedure where there is a lack of space.

DR. HENRY T. BURNS.—The advantages of this operation are becoming recognized and its popularity has increased rapidly during the past few years.

Fleischman and Kushner of the Bronx Hospital have recently reported a series of 19 cases with no maternal mortality.

Barnes of the Grace Hospital in New Haven has reported a series of 22 cases with no maternal deaths, and I believe he does the Latzko operation even as an elective procedure in some cases that have not been in labor.

In performing the Latzko extraperitoneal cesarean section 54 times, I have accidentally opened the peritoneum 7 times, but only once in the last 17 cases. I have never deliberately cut the peritoneum, but I can see where the method described by Aldridge may be of great help in very difficult cases. In getting the proper line of cleavage between the bladder and uterus, I have cut the endopelvic fascia transversely just below the peritoneal reflection, instead of longitudinally.

DR. JAMES F. NORTON (Jersey City, N. J.).—We have done 58 Latzko operations at the Margaret Hague Maternity Hospital in Jersey City. We have had one maternal death due to an injury to the patient's left ureter and subsequent death from sepsis. In the Margaret Hague Maternity Hospital, where we have a very large general service covering the entire County of Hudson, many patients are brought in that are impossible to handle in any manner except by some type of extraperitoneal operation.

I think that now practically all our operators isolate the posterior sheath of the endopelvic fascia in the same fashion as Aldridge has indicated. It was interesting to hear of Aldridge's method of handling the uterovesical fold of peritoneum. Cosgrove has utilized that procedure recently and he has gone so far in private conversation as to offer it as a modification of the technic of the Latzko section. I had not heard of it elsewhere until Aldridge described it tonight, but it has been utilized on the services in the Margaret Hague Maternity Hospital with no undue or untoward disturbances. We have not, as far as I know, used the vaginal type of drainage, all the patients being drained through the lower angle of the wound.

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**Ghosh, Datta and Adya: A Preliminary Observation on the Pharmacology of Ergometrine, J. Indiana M. A. 5: 519, 1936.**

Dudley and Moir in 1935 isolated an alkaloidal substance which differs from ergotoxine chemically and pharmacologically and which they named ergometrine. Almost simultaneously scientific journals in Britain, America, and on the Continent announced the isolation of a similar new alkaloid from ergot. They have been described under the names of ergometrine, ergotocin, ergostetrine, ergobasine, and ergometrinine.

The action of the new alkaloid differs from the alkaloid of the ergotoxine group in that the effects are produced in five to eight minutes when given by mouth, three to four and one-half minutes when given intramuscularly, and within a minute when given intravenously. The toxicity is low and no untoward symptoms follow its use over a prolonged period.

The authors conclude that: (1) Ergometrine has very little effect on the non-gravid uterus. (2) It causes powerful contractions of the gravid uterus but does not throw the uterus into tetany. (3) It stimulates the heart directly, making the beats stronger and quicker. (4) It causes a slight rise of blood pressure which, though not very high, is marked. (5) It has no gangrene effect like ergotoxine due to lack of peripheral vasoconstriction.

F. L. ADAIR AND S. A. PEARL.



## THE ENDOCRINE BASIS OF TOXEMIA OF PREGNANCY\*

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**I**N THIS paper we desire to present evidence to support our belief that the so-called toxemia of pregnancy is a manifestation of a disturbance of the endocrine glands.

The observations here recorded have been carried out over a period of four years. They have led to the conclusion that in the large majority of instances toxemia of pregnancy occurs in women with a constitutional habitus, in itself a manifestation of an endocrine disturbance.

Our primary criterion for the diagnosis of toxemia of pregnancy was the development in the later months of pregnancy of abnormally high blood pressure, in women in whom there was no history or other evidence of preceding renal or hypertensive disease. It may well be that there are cases of toxemia of pregnancy in which hypertension is absent and the disorder is manifested solely by edema and albuminuria. But in order to deal with a criterion of the disease which is practically universally accepted, we have included only patients with high blood pressure. All our patients began pregnancy with normal blood pressure and developed a systolic pressure exceeding 140 mm. and a diastolic pressure above 90 mm. Almost every patient had a blood pressure well over this level. The present study is based on 120 patients fulfilling this criterion. As controls, we have used 100 consecutive patients having normal pregnancies. The evidence is presented under the following headings: (1) Body weight, (2) hair distribution, (3) stature, (4) facies, (5) form of pelvis, (6) basal metabolism, and (7) blood proteins.

### 1. BODY WEIGHT

The pregestational weight of women with toxemia of pregnancy averages much more than that of a similar number of normal pregnant women (Fig. 3). The average weight in the normal series was 126.2 pounds, as contrasted to the average weight in the toxemia series of 148 pounds. The high incidence of obesity in patients who develop this disease is thus demonstrated. Moreover, in a large proportion of these cases there was a tendency to obesity from an early age. It is a well-known fact that patients with toxemia of pregnancy gain weight excessively. Further evidence indicates that this obesity is of endocrine

\*Read at a meeting of the New York Obstetrical Society, October 13, 1936.

origin and not due to gluttony or lack of exercise. For, in the first place, there was nothing to suggest that the food intake or exercise of the patients with toxemia differed from that of the controls; indeed, many of our patients were obese in spite of strenuous dieting. Second, there was a very high incidence of other endocrine stigmas in the obese individuals.

## 2. DISTRIBUTION OF HAIR

In the female, abnormalities in the distribution of hair resulting from endocrine disturbances are of two types: (1) An increase in the amount of hair, with a tendency to male distribution, that is on the legs, thighs, abdomen, chest, face, and occasionally around the nipples; (2) Decrease in pubic and axillary hair so that it is scanty, very fine and silky, and sometimes almost absent. These two types of abnormality in hair distribution due to endocrine disturbances were present, with almost equal frequency, in 74 per cent of the patients with toxemia, as compared to only 9 per cent of the normal controls.

## 3. STATURE

Various observers have noticed that a high proportion of women with toxemia of pregnancy are of stocky build. The coincidence of short, thick-set framework and obesity gives many of these women a characteristic appearance. There are some patients, however, that have an unusually large bony framework (Fig. 1). Definite abnormalities of stature were present in 65.8 per cent of the toxemia patients as contrasted with 21.0 per cent of the normal patients. It was found that the average weight/height ratio of patients in the normal series was 2.08 pounds per inch and that of patients in the toxemia series 2.5 pounds per inch (Fig. 4). Such peculiarities of stature are generally regarded as due to aberrations in the function of the endocrine glands.

## 4. FACIES

An outstanding characteristic of most of our patients with toxemia of pregnancy was that they looked several years older than their chronologic age (Fig. 2). Some young women of twenty to twenty-five years appeared thirty to forty years of age. This appeared to be due to the combination of obesity, statural peculiarity, and change in facies. They had enlarged features of the acromegaloid type, which in many were of long standing, and in others had appeared during the antepartum course. The most common change in the features was enlargement of the nose. These facial changes were sometimes associated with enlargement of the hands and feet. Their development was almost always noted by the patient or her companions, and often progressed noticeably under clinical observation. It is true that in normal pregnancy there is some enlargement of the features, generally attributed to physiologic hyper-

activity of the pituitary gland. This is rarely marked enough to become a complaint, as it was in some of our cases of toxemia of pregnancy. It was found that 55 per cent of the latter had changes in facies, whereas such changes occurred in only 5 per cent of the normal patients.

#### 5. FORM OF PELVIS\*

In the course of evaluating pelvic x-rays one year ago, we were aroused by the infrequency of the true gynecoid pelvis in those women who developed toxemia of pregnancy. Of 23 pelves in toxemic women, only 2



Fig. 1.



Fig. 2.

Fig. 1.—Showing stocky build and girdle obesity in a woman of twenty-six years, with toxemia of pregnancy. (Photograph taken two weeks postpartum after loss of 20 pounds.)

Fig. 2.—Facies of patient in Fig. 1.

were gynecoid. Since this observation, we have x-rayed routinely all patients who developed toxemia to determine the correlation, if any, between their body habitus and pelvic architecture (Table I).

The most striking feature of this survey is the low incidence of the gynecoid pelvis and the predominance of other types, especially the anthropoid. The table shows that the incidence of reversion to the male

\*We desire to express our sincere thanks to Drs. I. Seth Hirsch and Myron A. Schwartzchild for their aid with the roentgenologic aspects of this study.

and primitive type of pelvis in the toxemia series is very high. The rôle of the hormones in the evolution of pelvic types has been ably postulated by Caldwell, Moloy, and D'Esopo.<sup>1</sup> Since we find that women of extreme endocrine types in the great majority of cases have pelvises that fall into the android and anthropoid class, we may speculate that this reversion to the male and primitive type of pelvis is due to an inherent imbalance in the hormonal system.

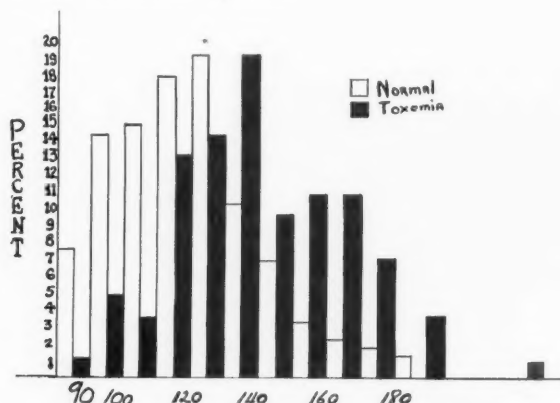


Fig. 3.—Pregestational weight of patients with toxemia and normal controls. Note the preponderance of toxemia among the obese.

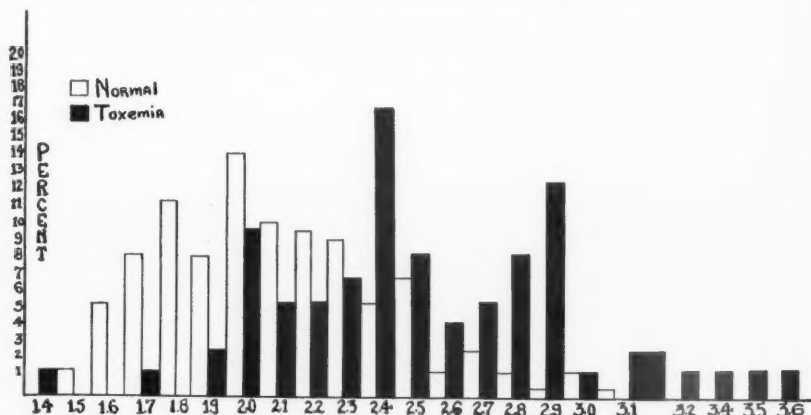


Fig. 4.—Pregestational weight/height ratio of patients with toxemia and normal controls, demonstrating the high incidence of obesity among the former.

We must further comment on the unusual number of large pelvises which appear to be more common than in our normal series. Some border on giantism, with dimensions far out of proportion to the stature of the patient (Fig. 5).

We wish to report a final observation relative to the separation of the symphysis during the antepartum period. Although the average separation, as seen stereoscopically, is not greater in the toxemia group than in the normal, in 7 cases this physiologic relaxation of the joint was by far

wider than any of a series of 150 normals (Fig. 6). In view of the accepted work of Abramson and coworkers,<sup>2</sup> this may indicate an abnormal endocrine function in these patients, although further observation on a larger series is necessary for verification.



Fig. 5.—X-ray of pubic arch of a large platypelloid pelvis. Note tremendous sweep of pubic arch and rami. Bis-ischial diameter 16.0 cm. Wide separation of symphysis (not demonstrable in this view) also present. Case of recurrent toxemia with marked endocrine stigmas.

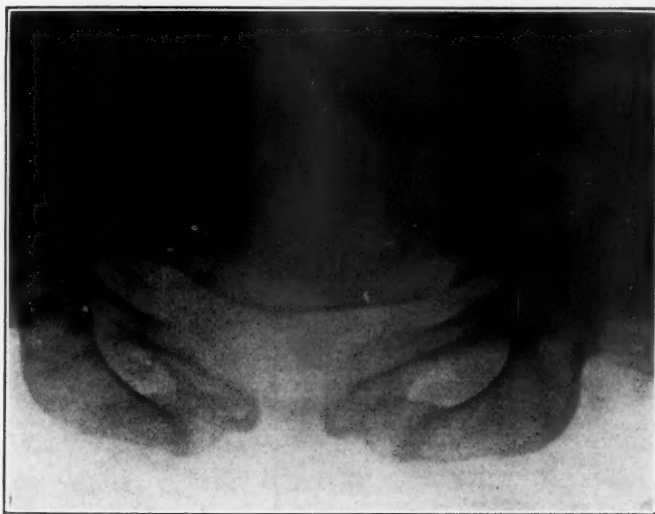


Fig. 6.—X-ray of symphysis in case of patient with toxemia, showing marked antepartum separation of symphysis. Patient of extreme endocrine type.

The observations on the form of pelvis thus add very strong evidence to the impression that toxemia of pregnancy occurs in a woman of definite constitutional habitus, due probably to dysfunction of the endocrine system.



## 6. BASAL METABOLISM

A number of investigators<sup>3-7</sup> have shown that in uncomplicated pregnancy the basal metabolic rate is increased 10 to 30 per cent above normal. This is especially true in the later months of pregnancy. It

TABLE I. SHOWING PELVIC TYPES IN THIS SERIES

TYPE	NUMBER OF CASES	PER CENT FOUND IN TOXEMIA	PER CENT FOUND BY CALDWELL, MOLOY AND D'ESOPH
Anthropoid	25	30.1	11.6
Gynecoid with anthropoid	13	15.7	4.6
Anthropoid with gynecoid	3	2.6	6.5
Android	14	16.6	11.6
Android with gynecoid	5	6.0	5.1
Android with anthropoid	8	9.6	3.7
Platypelloid	3		
Platypelloid with gynecoid	2	6.0	0.9
Gynecoid	6	7.2	39.5
Gynecoid with narrow forepelvis	4	4.8	11.1

should further be borne in mind, in this connection, that all our patients had high blood pressure, and it is well known to internists that in so-called essential hypertension there is a tendency to elevation of the metabolic rate. Hence, in hypertensive toxemia of pregnancy one would anticipate, a priori, a high basal metabolic rate by virtue of two factors, pregnancy and hypertension. It is, therefore, of interest and undoubtedly significant that in 35 patients with toxemia of pregnancy, in whom repeated observations of the basal metabolic rate were made, we found that 68 per cent had basal metabolic rates below plus 10 per cent, which is the accepted lower limit of normal during pregnancy (Table II).

TABLE II. SHOWING BASAL METABOLIC RATES IN CASES WITH TOXEMIA

CASE	PRIMIPARA	CASE	MULTIPARA	PER CENT BE- LOW +10%
1	+19	18	+13	Primipara
2	+30	19	+15	65%
3	- 3	20	-15	Multipara
4	+ 4	21	- 4	72%
5	+ 3	22	- 5	Total
6	+13	23	+15	68%
7	- 4	24	- 9	
8	- 8	25	+ 2	
9	+12	26	+15	
10	-10	27	+18	
11	+16	28	- 9	
12	-11	29	- 8	
13	+19	30	- 4	
14	- 3	31	+ 5	
15	+ 2	32	- 1	
16	- 2	33	- 2	
17	+ 3	34	- 3	
		35	+ 2	

Since the main control of the metabolic rate rests in the endocrine glands, such a relatively low metabolic rate is indicative of an endocrine disturbance.

In two instances, we had the opportunity of observing the development of toxemia of pregnancy, in patients following the fall in metabolic rate that took place, in the one instance "artificially" as a result of thyroidectomy, in the other spontaneously. The first patient was a primipara who had had a thyroidectomy for Graves' disease in the fourth month of pregnancy. Following this procedure, the basal metabolic rate, which had previously been high, fell to minus 20 per cent. This patient, who had had a normal blood pressure and urine, subsequently developed copious albuminuria and hypertension. The second case was also a primipara who had had a basal metabolic rate of plus 20 to 26 per cent on several occasions for two years prior to her pregnancy. Instead of increasing during the pregnancy, as it normally does, the basal metabolic rate fell to minus 3 per cent and she developed hypertension of 150/100 mm.

#### 7. PLASMA PROTEINS

Chemical studies of the blood in the toxemias of pregnancy have revealed a fairly constant abnormality in the concentrations of the plasma proteins. It has been definitely shown by many authors<sup>8, 9</sup> that the plasma proteins are diminished in these cases, and that this diminution is absolute and not due to dilution.<sup>10</sup> We corroborate these findings. In 15 of the 17 patients in whom this determination was made (Table III) the plasma protein concentration was depressed to between 4.07 and

TABLE III. SHOWING PLASMA PROTEIN DETERMINATIONS IN 17 CASES OF TOXEMIA, OF WHICH 1 TO 7 ARE PRIMIPARAS, THE REMAINDER MULTIPARAS

CASE	TOT. PROT.	ALBUMIN	GLOBULIN	A/G RATIO
1	5.51	3.05	2.46	1.2
2	4.07	2.61	1.46	1.7
3	4.68	2.25	2.43	0.92
4	4.93	2.39	2.54	0.9
5	5.20	2.50	2.70	0.92
6	4.25	2.81	1.44	1.9
7	4.68	2.34	2.34	1.0
8	5.06	2.81	2.25	1.2
9	5.20	3.75	1.45	2.5
10	5.91	3.51	2.50	1.4
11	5.51	3.12	2.39	1.2
12	6.25	3.95	2.30	1.7
13	5.51	2.73	2.78	0.98
14	5.85	3.12	2.73	1.2
15	4.93	3.21	1.72	1.2
16	4.93	2.34	2.59	0.9
17	6.25	3.12	3.13	1.0

5.91 gm. per cent as contrasted with normal limits of 6 to 8 gm. per cent. There was also inversion of the albumin/globulin ratio in 6 cases and a tendency toward inversion in 6 others. It is well known that abnormalities of the endocrines sometimes affect the level of the blood protein.

Since the depression in the protein content of the blood in some cases occurred without significant albuminuria or dietary deficiency, it seems probable that it was a manifestation of an endocrine disturbance.

#### TOXEMIA OF PREGNANCY AND RENAL FUNCTION

Parenthetically, we would like to interpolate a few words regarding the relation of toxemia of pregnancy to impairment of renal function. *In not one of 120 patients with toxemia of pregnancy was there significant impairment of renal function.* Of course, patients who entered pregnancy with glomerulonephritis are not included in the category of toxemia of pregnancy. Renal function was studied by the concentration test and by the determination of the nonprotein nitrogen of the blood. All the patients were able to elaborate urine of specific gravity 1.020 or more, which rules out significant impairment of renal function (see Fishberg).<sup>11</sup> The nonprotein nitrogen of the blood was also within normal limits. In the light of these facts, theories regarding impairment of renal function as a factor in the pathogenesis of the toxemias of pregnancy are, as has been realized by most recent students, to be discarded. Moreover, impairment of renal function need not be taken into consideration in the treatment of the toxemia of pregnancy. In the natural history of this disease, impairment of renal function does not appear during the pregnancy. It may appear after many years as a secondary consequence of the hypertension, just as it may result from long years of essential hypertension.

#### DISCUSSION

Summarizing the data just presented, it is found that 98 per cent of our patients with toxemia of pregnancy revealed evidence of one or more of the endocrine stigmas under consideration, and in a large majority there were two or more. The significance of these endocrine stigmas in women with toxemia of pregnancy is all the more evident on comparison with the normal controls. Only 15 per cent of the latter presented any endocrine stigmas and only 3 per cent had more than one stigma. The fact that 15 per cent of our normal controls presented endocrine stigmas does not militate against their significance in the toxemic cases. Our conception is that these stigmas are merely evidences of an endocrine disturbance, often constitutional in nature, which predisposes to the development of what is known as toxemia of pregnancy. That the actual disorder does not become clinically manifest in every individual with the underlying endocrine disturbance is not surprising, in fact would be anticipated, and has many analogies in clinical medicine. Of several sons of parents with diabetes and obesity, only some may actually develop glycosuria even though all are obese and show diminished sugar tolerance. The individuals with the endocrine stigmas described are al-

ways to be considered as potential victims of toxemia, which may develop only in one of their later pregnancies. This statement is borne out by the well-known fact that multiparas may develop toxemia despite previous normal pregnancies. The evidence here presented adds support to the theory that toxemia of pregnancy is a condition developing on the basis of a disturbance of internal secretion.

We do not feel that the observations here recorded throw any light on the precise nature of the endocrine disturbance which produces the toxemia of pregnancy. All the endocrine glands are interrelated and the function of all of them is affected in pregnancy. The available evidence does not permit a decision as to which of the endocrine glands is primarily at fault in the production of the toxemia of pregnancy. The work of Anselmino and Hoffmann,<sup>12</sup> purporting to show that the blood of patients with toxemia of pregnancy contains an excess of a pressor and antidiuretic principle secreted by the pituitary gland, has failed of confirmation.<sup>13</sup> On the other hand, the recent work of Smith and Smith,<sup>14</sup> revealing the presence of an excess of prolactin in the toxemia of pregnancy, is carefully controlled and to be accepted; it may well prove the starting point of more intimate knowledge of the nature of the endocrine disturbance underlying the toxemia of pregnancy, but does not as yet show how this disturbance is initiated.

#### THERAPEUTIC AND PROPHYLACTIC IMPLICATIONS

Since the large majority of cases of toxemia of pregnancy develop in women who present detectable evidences of endocrine dysfunction, one has a basis in the antepartum clinic for the segregation of those women who are most likely to develop toxemia. Our observations indicate that about 30 per cent of women presenting the endocrine stigmas described above (stocky framework, obesity, abnormal distribution of hair, etc.) will develop toxemia of pregnancy. In the past six months we have observed 34 women with such endocrine stigmas but no evidences of toxemia develop definite toxemia of pregnancy. We feel that if women with endocrine stigmas are segregated in antepartum clinics and carefully watched, one will observe the inception of the vast majority of cases of toxemia of pregnancy. This will afford the opportunity not only to undertake appropriate measures of therapy at the time when they are most useful, but also to study the pathogenesis of this disease.

The following may be said regarding the therapeutic implications of the fact that the toxemia of pregnancy is a result of endocrine dysfunction. While the precise nature of the endocrine disturbance is unknown, it is manifested by water retention in the organism. This water retention not only produces palpable edema, but it also may go on to the edema of the brain which is concerned in the production of the eclamptic

seizure. In our hands the most efficient treatment of the toxemia of pregnancy has been a regimen which tends to dehydrate the organism. The patient is put on a salt poor diet and the fluid intake is restricted to 1,000 c.c. or less. What is especially to be emphasized is that protein intake is not limited; in fact, especially in patients with considerable albuminuria, we give as much as 100 gm. of protein daily. It should be remembered that the plasma proteins are generally low in the toxemia of pregnancy, and this favors the formation of edema; ample protein intake is essential to combat the lowering of the plasma proteins and thus tend to avert or remove edema. There need be no fear of nitrogen retention because of the high protein intake; renal function is not significantly impaired. Other dehydrating measures which we employ are the frequent administration of magnesium sulphate by mouth with resultant abundant watery stools and the use of thyroid extract in those cases having a low basal metabolic rate. The latter is indicated not only by the tendency to water retention, which it combats, but by the relatively low basal metabolism. The usual bed rest and mild sedation with chloral and bromides or phenobarbital are also employed. In patients with great hypertension in whom convulsions or other cerebral symptoms seemed to impend, or with actual eclamptic convulsions, we have found the intravenous administration of magnesium sulphate of great value in addition to the other usual routine procedures.

Using the "dehydrating regime" just described, we have obtained splendid results in the large majority of patients with so-called pre-eclampsia, with clearing up of edema and fall in blood pressure. In the past four years convulsions did not develop in any patient with pre-eclampsia treated by this regime in our service at the Jewish Maternity Hospital. However, we should like to emphasize the fact that we do not believe that patients should be "carried along" on a medical regime for a long time. Our findings corroborate the important studies of Harris,<sup>15</sup> Peckham,<sup>16</sup> Corwin and Herrick,<sup>17</sup> and Herrick and Tillman,<sup>18</sup> who have shown that a high proportion of patients with toxemia later develop hypertensive disease with resultant shortening of life. There is some reason to believe that the chances of developing hypertension in later life are augmented by allowing the toxemia to persist for too long a period. For the sake of the mother later in life, she should not be allowed to remain in a toxemic state any longer than necessary.

#### CONCLUSIONS

Evidence is presented which, we believe, indicates that toxemia of pregnancy is an endocrine disturbance evolving in women with a pre-existent constitutional abnormality of the endocrine glands. The evidence consists in the following:



1. The average prepregnancy weight of patients that developed toxemia is 21.8 pounds more than that of patients in the normal series. The incidence of obesity in this type is great.
2. A high percentage of women with toxemia have abnormal distribution of hair.
3. Sixty-five and eight-tenths per cent of patients with toxemia have abnormalities of stature as contrasted with 21 per cent of controls. The average weight/height ratio of the normal series was 2.08 as compared to that of 2.5 for the toxemia series.
4. Fifty-five per cent of women with toxemia had changes in facies of the "acromegaloid" type as contrasted with 5 per cent of the controls.
5. Eighty-eight per cent of our cases with toxemia showed reversion to the male and primitive type of pelves. Giant pelves were unusually frequent.
6. Basal metabolic rate in toxemia of pregnancy averages definitely less than in normal pregnancy.
7. As has previously been demonstrated by others, the plasma proteins in toxemia of pregnancy are depressed below those in normal pregnancy.
8. In 98 per cent of our patients with toxemia of pregnancy there were one or more endocrine stigmas, and in a large majority there were two or more. Only 15 per cent of the normal controls presented any endocrine stigmas and only 3 per cent had more than one stigma.
9. In not one of our series of 120 cases of toxemia of pregnancy was there significant impairment of renal function as demonstrated by the concentration test and by the determination of the nonprotein nitrogen of the blood.
10. All pregnant women having endocrine stigmas should be considered as potential victims of toxemia. It is advised that they be segregated for investigation and proper therapy. The latter consists mainly in a regime of dehydration.
11. In "carrying along" a patient with toxemia of pregnancy, the fact should be seriously considered that a high proportion of patients later develop hypertensive disease with resultant shortening of life.

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## DISCUSSION

DR. RAPHAEL KURZROK.—The whole subject of the interrelationship between the endocrine glands and toxemia of pregnancy was, I believe, first noted about twenty years ago, by Hofbauer. He, at that time, postulated the theory that the pituitary gland and the adrenals in association with a placental factor, the so-called biogenous amines, substances of high pharmacologic potency, were interrelated with the toxemia of pregnancy. Only the first part of his theory has been taken up and investigated.

Among the symptoms of toxemia, hypertension and edema are notable, as the result of a hyperproduction of one or possibly two of the hormones of the posterior pituitary gland. In the posterior pituitary gland we have a group of hormones, one of which, oxytocin, has to do with the contraction of the uterus, and has no bearing on the problem at hand. The other has a combination of activities, probably residing in two molecular groups: the first raises the blood pressure, the second inhibits diuresis. Another substance, possibly arising from the middle portion or the pars intermedia of the pituitary gland, has an effect on the melanophore groups of certain species. Anselmino and Hoffmann stated that the retention of water and the hypertension can very well be due to an overproduction of the hormone which produces exactly these two phenomena and whose origin is in the posterior pituitary gland. Unfortunately, they worked with the rabbit, which is notoriously unreliable, especially so far as this particular type of testing is concerned.

The next important advance in this field was made by Cushing, who noted, in six cases of eclampsia, that there was direct invasion on the part of basophilic cells from the anterior pituitary gland and pars intermedia into the posterior pituitary gland, and that in the invasion of the posterior pituitary gland these cells underwent a process of degeneration and formed the amyloid substances or Herring bodies. He postulated, in addition, that the substance, vasopressin, arises from the anterior pituitary gland, because histologically, the posterior hypophysis does not appear like a secreting tissue. This view is of importance, because the anterior pituitary is that portion which enlarges during pregnancy. Cushing's concept has, however, recently been attacked in the work of Geiling and Lewis, and others. They have demonstrated that pure tissue cultures from the anterior pituitary gland contain neither the substance that raises blood pressure nor the substance that inhibits diuresis, nor the melanophore-expanding hormone. On the contrary, pure tissue cultures, arising from the posterior pituitary gland, produced both vasopressin and the melanophore-expanding substance.

The other work which has been amazingly interesting in this field has been that of Smith and Smith of Boston, who demonstrated that in true toxemia of pregnancy there is a marked increase in the amount of prolactin and a lowering in the amount of estrin of both the blood and the urine. At the present time we do not know whether the increase in prolactin is a cause, or the result, of toxemia. It is very interesting to note that the lowering of the plasma of proteins is a usual concomitant of a lowered basal metabolic rate which has been found to accompany most of these cases of toxemia of pregnancy.

More recently the adrenal has been drawn into the picture of toxemia of pregnancy by Fauvet. The adrenal is one of the glands of internal secretion that markedly enlarges during pregnancy. In toxemia of pregnancy and especially in eclampsia, however, there is a distinct diminution in the size of the cortex of the adrenal, and possibly some cases of death from toxemia of pregnancy unassociated with convulsions, may be due to a failure on the part of the adrenal.

The general concept that offers the most potent possibilities is perhaps one comparable to, but opposite in effect to, our view of the menopause. The menopause is due to a derangement of the glands of internal secretion because of the permanent

loss of one of these glands (the ovary). On the other hand, in pregnancy, a new gland of internal secretion in form of the placenta has been added. A re-arrangement must take place, the nature of which depends a great deal upon the individual's constitutional make-up, and endocrine equilibrium. Hence, the derangement thus induced in the pregnant woman will vary from patient to patient. In one it may be an overstimulation of the posterior pituitary gland, in another a failure of the adrenal cortex (hyperemesis?), in a third hyperthyroidism, in a fourth a tachycardia due to disturbance of the autonomic nervous system, etc.

DR. ROBERT T. FRANK.—No one can take exception to the extremely interesting clinical type presented this evening. The numerical preponderance of this group may be of significance, although the stigmas presented are very common. That they should appear in such numbers in this group proves at least that these individuals are more easily affected by disturbances, the nature of which I am unwilling to attempt to analyze, than other groups. If these gentlemen will take the time and the trouble, because much is involved, to study this group further, it would be important to note whether they are equally subject to other disturbances. If this were true, it would merely mean that these individuals are more readily affected by many kinds of trauma, including eclamptic poisoning, if you wish to call it that. The speakers have wisely refrained from attempting to state what is the basic cause of eclampsia. All you can say is that this group certainly shows what the Germans call "Minderwertigkeit," a weakness, a vulnerability to the disturbance.

DR. ARTHUR W. BINGHAM.—Dr. Langrock has described cases of patients who are, as we all know, more likely to become toxic, and who are poor risks medically and surgically as well as for maternity. That does not explain, however, the case of the average healthy young woman who eats too much, sits around, and does not exercise, gains too much weight, and develops a disturbance in her metabolism, endocrine glands and water balance. The question is how to prevent toxemia in the average healthy young woman.

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## A STUDY OF DERMOID CYSTS WITH A SUGGESTION AS TO THE USE OF X-RAY IN DIAGNOSIS\*

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**S**EVENTY-NINE patients with dermoid cysts of the ovary were admitted to the Long Island College Hospital from October, 1923, to May, 1936. Analysis of these cases emphasizes certain features which have considerable clinical significance. The youngest patient was fifteen years of age and the oldest fifty-eight. Sixty-five, or 82 per cent, were observed between the third and fourth decades of life.

Among 500 consecutive ovarian neoplasms removed during this period, dermoid tumors ranked second to the serous cystomas which constituted one-third of our material and, surprisingly, they were more common than the pseudomucinous cysts which were noted in only 9.2 per cent of the cases.

\*Presented (by invitation) before the New York Obstetrical Society, November 10, 1936.

## PATHOLOGY

The right ovary was the site of the newgrowth in 33 instances, the left in 34. Both sides were involved in 12 or 15.2 per cent of our patients. As a result 91 specimens were available for study. Since the opposite ovary had been removed previously for a dermoid in two women, bilateral involvement really occurred in 14, or 17.7 per cent, of our cases. The smallest tumor was 4 mm. in diameter and the largest measured 40 by 25 cm., their average size being 9.5 cm. The contents of the cyst cavities were as follows: sebaceous material and hair in 81, sebaceous material alone in 6, and only hair in 2. One cavity was filled with hair mixed with a gelatinoid material. Seventy-three tumors showed the characteristic anlagen. These included calcareous substances, such as teeth in 18, bone in 13, and teeth in combination with bone in 8. Therefore, 39, or 49.4 per cent, revealed calcareous deposits. It was interesting to note that in none of the bilaterally involved cases was calcium seen in both ovaries. On microscopic examination, the well-differentiated adult structures which have been described frequently were demonstrated (Fig. 1). We encountered thyroid tissue in 9 cases and in one instance it was present on both sides (Fig. 2). The frequent association of pseudomucinous cysts with dermoids, noted by Blair-Bell<sup>1</sup> and Shaw,<sup>2</sup> was not observed in our material. We had but one case. The most common associated pelvic pathology was multiple fibroids of the uterus which occurred in 17.7 per cent. This figure corresponds with the expected frequency of fibroids in any gynecologic series.

## SYMPTOMATOLOGY

In reviewing the literature, one is impressed by the varying opinions concerning the symptoms produced by these neoplasms. Lynch<sup>3</sup> attributes little significance to the symptoms of dermoids. He states "symptoms might be slight or absent, though occasionally the patient may sense a weight in the pelvis, or complain of bladder and rectal discomfort." In Table I, the symptoms noted in Marshall's<sup>4</sup> 415 cases are compared with those in our series.

TABLE I

	CASES	LOWER ABD. PAIN	BACK- ACHE	PRESSURE ON BLADDER OR RECTUM	TUMOR MASS	MENSTRU- AL ALTERA- TION
Marshall	415	48.0%	18.0%	27.0%	23.5%	12.0%
L. I. C. H.	79	65.5%	17.6%	30.6%	12.6%	7.5%

The frequency of pain and pressure, we feel, is due to the effect of the size, the location, and the relation of the tumor to other structures. The vast majority of dermoids grow slowly, and as a rule, reach moderate size. Their average diameter, in our material, was 9.5 cm. Due to their weight they usually remain in the pelvis, but because of their long pedicle, marked mobility is possible and as a result they frequently lodge in either the anterior or the posterior culdesac. This localization of the tumor in the pelvis often is aided by their becoming densely adherent to either the rectum or the bladder. Hence by virtue of their position, lower abdominal pain with pelvic pressure is to be expected. The long pedicle also permits displacement upward into the abdominal cavity with sufficient force to permit its recognition by the patient and spontaneous dislocation is often produced by sudden changes in posture. This was noted in 10, or 12.6 per cent, of the cases.

Menstrual disturbances were rare. In five, amenorrhea was due to an associated pregnancy. Five other patients complained of irregular bleeding while one experienced polymenorrhea. This lack of menstrual abnormalities may be explained by

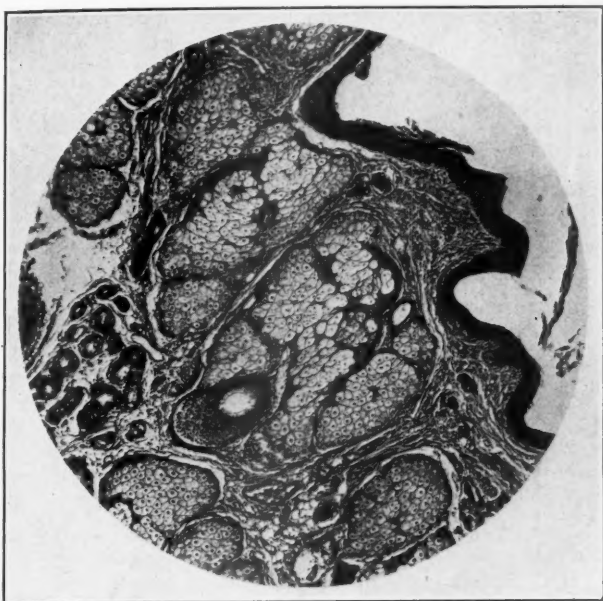


Fig. 1. Section taken through a dermoid anlage presenting adult squamous epithelium beneath which are many cross-sections of sebaceous glands, sweat glands, and hair follicles.

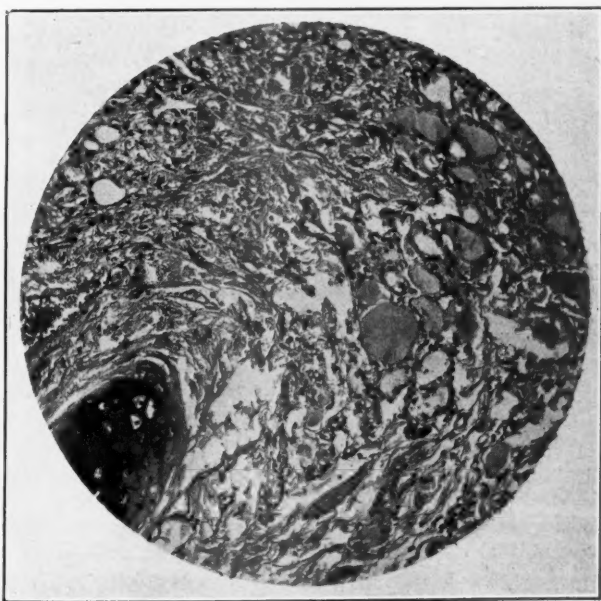


Fig. 2.—This section has been taken through a dermoid cyst, revealing a segment of adult hyaline tissue surrounded with typical thyroid tissue.



the fact that these tumors usually contained a compressed segment of ovarian parenchyma sufficient to maintain the cycle. Marked changes in menstruation accordingly occur only late in the course of the tumor's growth.

#### COMPLICATIONS

Twenty-one of the specimens were insignificant in size. Only 70 of the tumors studied, therefore, were capable of producing complications, the relative frequency of which is shown in Table II.

TABLE II

	NO. OF CASES	PER CENT
Adhesions	16	23.0
Torsion	15	21.4
Pelvic abscess	1	1.4

As torsion was associated with adhesions in three and in one of these a coincident infection was also observed, 29, or 41.4 per cent, of our patients developed one or more complications. Two small dermoids were found in conjunction with ovarian carcinoma, but these were considered as concomitant findings.

In 16 instances the tumor was adherent to other pelvic organs. Ten of these patients complained of abdominal pain, thus substantiating the statement that abdominal pain occurs most frequently as the result of adhesions. This complication may be produced by the irritating contents of the cyst, and the late Dr. Polak noted that peritonitis was prone to follow intraabdominal rupture of a dermoid.<sup>5</sup> In one of our patients, rupture during extirpation resulted in the formation of adhesions sufficiently dense to cause intestinal obstruction.

When adhesions develop, the tumor usually becomes fixed to the rectum or the bladder. This favors the transmission of pathogenic bacteria via the lymphatics into the cyst, and the secondary infection thus produced may give rise to a pelvic abscess. In one patient a posterior colpotomy was done for such a pelvic abscess, and the correct diagnosis was made only when teeth were discharged through the colpotomy incision.

#### TORSION

Dermoids are prone to undergo torsion. The incidence of its occurrence in our clinic as well as in the material reported by other writers is given in Table III.

TABLE III

	NO. OF DERMIDS	NO. SHOWING TORSION
Shaw	23	3
Sänger	33	6
Furlong	50	5
Long Island College Hospital	70	15
Konehy	100	12
Sterer	248	43

The greatest number of twists found in the pedicles of our 15 cases complicated by torsion was six. Free fluid in the abdomen was noted in two. Eleven patients complained of abdominal pain which in four instances was brought on by a change in posture. Four women complained of nausea and vomiting, while three felt a tumor mass. Nine of the tumors which had undergone torsion were in the anterior culdesac, two in the posterior culdesac, one in the right fornix, and only one was in the abdominal cavity. In the remaining two, the location of the tumor was not recorded. These observations are unusual, for torsion is held to be more common

in the abdominal rather than in the pelvic phase. The laboratory data were insignificant except in this group, 9 patients of which had a leucocyte count of more than 10,000. In one, the temperature was elevated to 99.6° F.

#### MALIGNANT CHANGES

Two small incidental dermoids were found in conjunction with ovarian malignancy. One was an embryonal carcinoma and the other accompanied a papillary cyst adenocarcinoma. Neither carcinomatous nor sarcomatous change was present in any of the cases.

#### DERMOIDS WITH PREGNANCY

Five of our cases were associated with pregnancy. Two presented no symptoms and were recognized for the first time during the initial prenatal examination. The remaining three complained of abdominal pain. One patient experienced a rapid increase in the size of her abdomen though she knew herself to be but three months pregnant. Pregnancy is said to favor torsion in dermoids.<sup>7</sup> Theoretically, the enlarging pregnant uterus alters the position of the tumor, and as it is elevated into



Fig. 3.—X-ray revealing well-formed teeth in the left ovary which is the seat of a dermoid tumor.

the abdominal cavity a twisting of the pedicle may occur. Among our five pregnancy cases, however, the tumor was located in the abdominal cavity above the uterus in but one, while the remaining four were found twice in each of the cul-de-sacs. Complications were noted in three cases. One tumor was twisted, and one covered with adhesions. In the third patient, the tumor was incarcerated in the pelvis in front of the fetal head. A cesarean section was done, because it was felt that labor might rupture the cyst, or the tumor itself might cause dystocia. At operation the head was floating and the dermoid was deeply incarcerated in the pelvis.

Fifty-seven patients had been pregnant one or more times. That sterility is not influenced by dermoids even when they are bilateral has been shown by Manton who collected 19 cases of pregnancy associated with bilateral tumors.

#### DIAGNOSIS

The diagnosis of dermoid cyst is rarely made (Counsellors<sup>8</sup>). This statement was borne out in Marshall's series where the correct diagnosis was never made with any degree of certainty, though suggested in a few instances. In our group, it was diagnosed seven times and in one, this was the result of x-ray examination. In the

remaining cases the preoperative impressions were as follows: Ovarian cyst in 41; fibroid uterus in 21; adnexitis in 7; and in each of the remaining 3, pelvic tumor, hydrosalpinx, and pelvic abscess, respectively, were suspected.

In spite of all that is said to the contrary, a correct preoperative diagnosis should be made more frequently. The vast majority of dermoids are found in the pelvis. In 61 cases where the location was noted, 60 were in the pelvis and only 1 was free in the abdominal cavity. Of those in the pelvis, 39, or 64 per cent, were situated either in the anterior or the posterior culdesacs. The sebaceous material commonly encountered within the locule, intermingled with teeth or bone, produces characteristic areas of pultaceous and solid consistency which are demonstrable on palpation, particularly when the tumor is in the pelvis.

The neoplasms in 39, or 49.4 per cent, of our 79 patients contained calcareous substances, a higher incidence of this finding than is ordinarily reported. Excluding the urinary tract, radiopaque shadows in the female pelvis other than phlebolites, are uncommon, and are due to calcified areas in a fibroid uterus, a lithopedion, calcified lymph nodes, or a dermoid cyst (Fig. 3). According to Dr. A. L. L. Bell, Radiologist of the Long Island College Hospital, a correct interpretation of the shadows due to the calcareous structures within a dermoid cyst can usually be made. We feel that a higher incidence of correct preoperative diagnoses could have been made in our series had the x-ray been used more frequently. We therefore strongly advise the use of the x-ray whenever the anterior position of a pelvic tumor, or its feel on palpation, suggests a dermoid cyst.

#### TREATMENT

The frequency with which these tumors undergo complications makes it advisable that they be extirpated as soon as the diagnosis is made. Oophorectomy is always indicated in unilateral dermoids. Since 17.7 per cent of our cases showed bilateral involvement, both ovaries should be removed whenever this is not contraindicated by the age of the patient. In a young woman, if the opposite ovary is enlarged, or if a zone of hardness is felt, the organ should be hemisected and searched for a small dermoid locule. Should one be encountered, its enucleation is indicated. Bilateral dermoids are best handled by double oophorectomy. On the other hand, if the patient is young, resection of the ovary least involved may be substituted, a procedure which has been done successfully in a number of cases. The possibility, however, of the usual sequelae of resection must be considered. In this connection, it may be stated that the increasing knowledge of ovarian substitution therapy in artificial menopause makes the decision less difficult.

As a rule the immediate postoperative course was uniformly good and the majority of our patients were discharged from the hospital at the end of fourteen days.

#### FOLLOW-UP

Four patients in our series died. In two, small dermoids were found in conjunction with ovarian malignancies which caused fatal carcinomatosis seven and twelve months after operation. One patient died three days postoperatively of myocardial failure. The fourth death resulted from cardiac decompensation and bronchopneumonia fourteen days after operation. The corrected mortality is 2.5 per cent.

Our follow-up consists of 61 patients seen ten months to nine years following operation. In short, the pelvic findings and symptoms noted during these examinations are too few and varied to warrant any discussion.

It is significant, however, that 7 patients subsequently have delivered full-term normal infants, and 2 were gravid at the time of their last examination.

## SUMMARY

1. There were 15.8 per cent of 500 consecutive ovarian tumors which were dermoid cysts.
2. Eighty-two per cent occurred between the third and fourth decades.
3. In 15.2 per cent both ovaries were involved at the time of admission, and two patients previously had the opposite ovary removed for a dermoid, so that 14, or 17.7 per cent, actually had bilateral involvement.
4. In 29 instances adhesions, torsion, or infection were encountered as complications.
5. Five cases were associated with pregnancy. Follow-up also showed that 9 of our patients became pregnant subsequent to a unilateral oophorectomy.
6. The postoperative course and follow-up in the majority of cases were uneventful.
7. The corrected mortality was 2.5 per cent.
8. Teeth or bone, alone or in combination, were encountered in 39, or 49.4 per cent, of our cases. Had x-ray been used more frequently, a high percentage of these tumors could have been diagnosed before operation.

We wish to express our sincere thanks to all the members of the Gynecological Staff for their cooperation and kindly suggestions.

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## DISCUSSION

DR. SAMUEL A. WOLFE.—In our series at the Long Island College Hospital we encountered no secondary malignant changes in the dermoid itself. Carcinomas have been described in the epidermoid lining, the frequency being estimated at about 1 per cent.

The clinical problem of bilateral dermoids in young women, particularly those desiring children, is one of great importance. Where there are multiple dermoid locules, it is almost impossible to conserve any segment of ovarian parenchyma, but care and persistence will reveal a segment which can be retained to continue menstruation and fertility.

In our series of dermoids, segments of thyroid tissue were frequently seen on microscopic examination. In two, however, the thyroid tissue practically obscured all other elements, and a diagnosis of struma ovarii was properly made. In both cases the thyroid showed no evidence of secondary malignancy or hyperplasia and signs of thyroid intoxication were lacking.

DR. VINCENT P. MAZZOLA.—The following case will emphasize the use of the roentgen ray in the preoperative diagnosis of dermoids, a procedure of particular value in the case of children where the diagnosis of abdominal tumors is difficult.

A child about five years old was admitted to my service at St. Peter's Hospital, complaining of epigastric pain, vomiting, and an abdominal tumor. On examination, she presented a tumor mass about 7 cm. in diameter in the epigastrium. The tumor was semicystic, freely movable and not tender. An abdominal flat x-ray plate was taken which revealed a tumor mass containing opaque substance which resembled rudimentary mandible and teeth. The diagnosis of dermoid cyst was made and confirmed at operation. (Slides showing the gross appearance of the tumor and the roentgenograms before and after removal from the abdomen.)

DR. FRANK R. SMITH.—At the Memorial Hospital we have a rather distorted distribution of types of ovarian tumors. The dermoids formed only about 8 per cent of all ovarian tumors. The distortion is shown by the fact that in 1932, in reviewing a series of 376 patients with ovarian tumors, I found that only 54 were benign. You get a further idea of our distortion when you appreciate that 78 per cent of patients with malignant tumors had been operated upon previously, coming to us after either an incomplete operation or simple exploratory celiotomy.

For some time we have been interested in x-raying certain ovarian tumors, perhaps with the idea of seeing if we could diagnose them as dermoid cysts. Yet even when suggestive shadows were present, some of our guesses have been wrong. Two patients with missed abortion, one with retention of a fetus for twenty years and the other for nine years, were each regarded by at least one x-ray man as having a dermoid cyst.

It seems to me that this is an academic study rather than a practical one, for it is hard for me to conceive of an ovarian tumor that does not require operation. Its only value may be to decide whether a given case is to be referred to a surgical or gynecologic service.

142 JORALEMON STREET  
340 HENRY STREET

## RUPTURE OF GRAAFIAN FOLLICLES

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*(From the Maternity Hospital, Cleveland, and the Medical Department of Western Reserve University)*

WHILE doing Friedman tests for pregnancy, the phenomenon of the rupture of the ovarian follicles excites one's interest. We wonder at the mechanism which causes these tiny blebs, after lying almost dormant for the whole life of the female, to swell up and burst within the course of a few hours under the influence of what we call a hormone. We have reported previously the actual observations of this process.<sup>1</sup> The peritoneal cavity of a rabbit was opened nine hours after an injection with the urine of a pregnant woman. The whole cavity was expanded, and filled with warm mineral oil, following the technic of Dr. E. E. Ecker.<sup>2</sup> At that time, some follicles were already markedly swollen. They increased slowly, until finally the thin area at the stigma ruptured, releasing a trickle of follicle fluid and blood into the surrounding oil. The first follicle ruptured ten hours and twenty-six minutes after the injection of urine.



Several theories have been proposed to explain this mechanism of rupture.<sup>3</sup> We feel that, if we hope ever to understand the action of hormones, an important first step is to find out just what changes they cause in the follicles of the ovary. The formation of the *corpora hemorrhagica* is merely a result of these changes. There are three main theories as to the cause of this rupture:

1. Smooth muscle fibers in the ovarian stroma contract rhythmically, and squeeze the tense follicle. But there is little histologic evidence for the presence of such fibers in the ovary. In our observations under oil, in spite of the closest watching, no sign of motility could be detected in the ovary.

2. An enzyme digests the internal lining of the follicle wall until it is too weak to resist the fluid pressure. There seems to be little direct evidence for this view. On pressure, a follicle about ready to rupture seems fully as tough as does one that has not been stimulated.

3. Increased intrafollicular pressure, due (a) to change in the osmotic tension of the fluid, or (b) to liquefaction of the cells in the so-called bodies of Call and Exner. At the time we observed the follicles under oil, one could not but be impressed by the evidences of increased internal pressure. The follicles swelled up, enlarged, projected above the surface of the ovary, and showed every appearance of being tense. When such a follicle was tapped with a capillary glass tube, the fluid rushed up faster and higher than did the fluid drawn from an unstimulated follicle into a similar tube.

How could the osmotic tension of such a tiny amount of fluid be estimated? After many efforts, we tried a vapor tension method described by Walker.<sup>4</sup> This was used by White for comparing the molecular concentrations of urine and of plasma in kidney glomeruli. We drew three droplets, separated by air spaces, into a glass capillary tube. The first and third droplets were distilled water. The central drop was the fluid to be tested. Hygroscopic substances present in that central droplet will cause it to take up water from the vapor in the air on each side of it. Thus, such a droplet will increase in length. Rather to our surprise, we found that it actually does so increase to a very measurable extent. As soon as made up, the ends of the tube are sealed with paraffin; and the length of the central droplet is measured, lying upon the grating of a blood corpuscle counter (Fig. 1). The length of the drop is again measured after twenty-four hours. As it proves technically impossible to get the drops in different tubes of exactly the same length, or even to get capillary tubes of exactly the same caliber, the increase in length is expressed in *percentage* of the original length of the droplet. After numerous experiments, it was found possible to fill the capillaries by means of the apparatus illustrated (Fig. 2). The bulb of an eye-dropper, held in a hinged clamp, can be compressed or relaxed accurately with the pressure of a finger. A tube connects the dropper nozzle with a solid rubber cap of a vaccine ampule. Through

this cap the capillary glass tube is thrust, as a hypodermic needle is thrust when removing a dose of vaccine from its bottle.

A series of such capillary tubes was set up, using for the central drops salt solutions of known concentration. Notwithstanding some eccentric observations, the increase in droplet size followed the amount of salt in the solution surprisingly. The results are given in Table I. Put on coordinate paper, the horizontal distance repre-

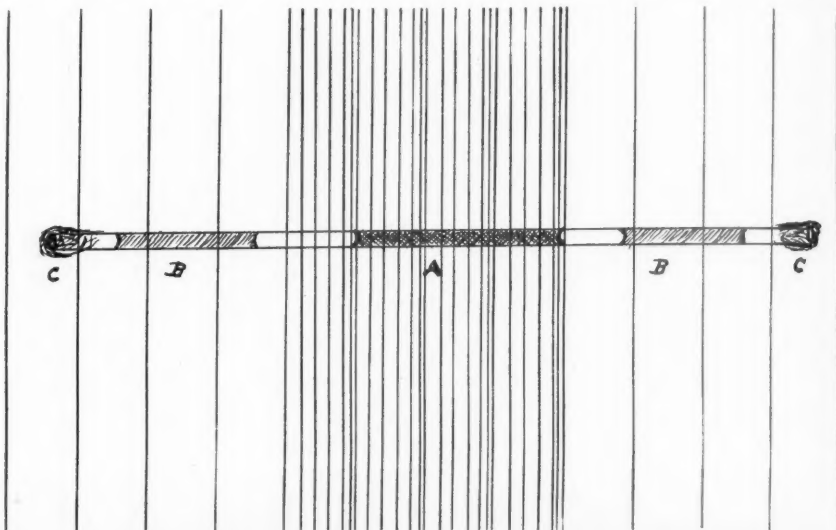


Fig. 1.—Capillary tube, on grating, for measuring length of central drop. (To avoid confusion, cross lines of grating are not shown.) A, Droplet of fluid to be tested. B,B, Distilled water droplets. C,C, Paraffin seals. (Magnification, 1-40.)

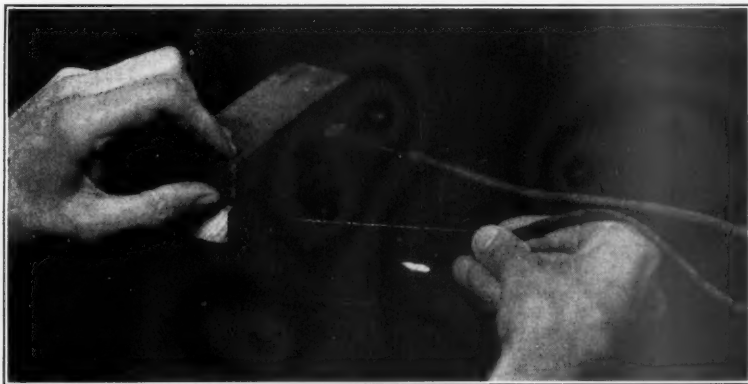


Fig. 2.—Apparatus used to draw fluid into capillary tubes.

sents the *percentage* increase in the drop length, while the vertical distance shows the *percentage* of salt in the central droplet. This is illustrated in Fig. 3. A line run through the mean of the observations at each saline *percentage* tested seems to approximate more to a curve than to a straight line. However, this effect may be a false one caused by the drawing of the curve far to the right on the 0.85 per cent ordinate by a few very erratic observations which are probably incorrect.

After this curve had been estimated, the next step was to take fluid from swollen, but not ruptured, graafian follicles of rabbits ten hours after they had been injected with the urine of a pregnant woman. At the same time, to avoid any differences that temperature changes might cause, capillary tubes were also set up containing fluid from mature follicles that had not been stimulated by injection. In taking these droplets, the greatest care must be exercised lest the glass tube

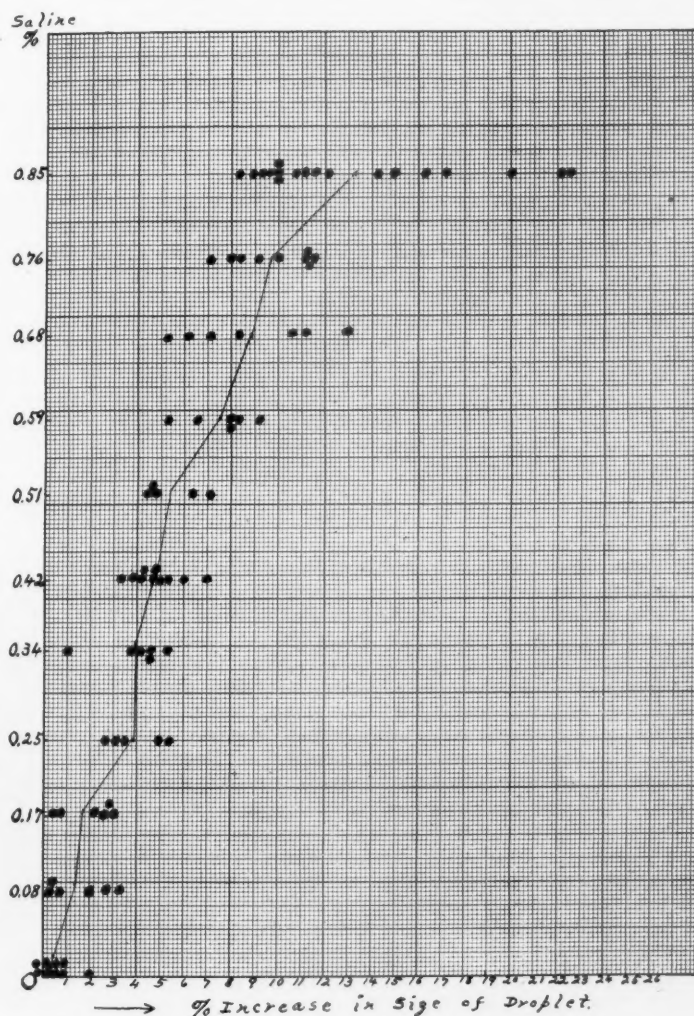


Fig. 3.—Expansion of droplets of known concentration of NaCl.

penetrate too far into the tiny follicle, injure the capillary bed on the under-side, and contaminate the fluid with blood. There certainly was a definitely different, if slightly erratic, rate of lengthening in the two sets of droplets. Table II shows the results.

We have drawn on coordinates the same curve we derived from the means of the salt drops of known concentration. On this curve, we have interpolated the results from the observations on the follicle droplets, where their rate of expansion line

TABLE I. CAPILLARY EXPANSION OF DROPS OF VARYING KNOWN CONCENTRATION OF NaCl

PER CENT SALINE	DROP LENGTHS, EXPRESSED IN $\frac{1}{20}$ MILLIMETERS		PER CENT CHANGE
	AT START	AFTER 24 HOURS	
0.85	22	27	plus 22.6
	90	99	plus 10.0
	17	21	plus 22.2
	28	32	plus 14.2
	40	46	plus 15.0
	35	40	plus 14.3
	51	56	plus 9.8
	48	52	plus 8.3
	46	51	plus 10.8
	43	48	plus 11.6
	43	47	plus 9.3
	30	33	plus 10.0
	39	43	plus 10.0
	33	37	plus 12.1
	44	52	plus 20.0
0.76	27	30	plus 11.1
	42	45	plus 7.1
	26	29	plus 11.5
	36	40	plus 11.1
	50	55	plus 10.0
	36	39	plus 8.4
	50	54	plus 8.0
	55	60	plus 9.1
	18	20	plus 11.1
0.68	28	31	plus 10.7
	36	40	plus 11.1
	23	27	plus 13.0
	48	52	plus 8.3
	65	69	plus 6.1
	28	30	plus 7.1
0.59	37	40	plus 8.1
	25	27	plus 8.0
	38	40	plus 5.3
	24	26	plus 8.3
	45	48	plus 6.7
	38	40	plus 5.3
0.51	46	48	plus 4.4
	45	47	plus 4.4
	14	15	plus 7.1
	62	65	plus 4.8
	31	33	plus 6.4
0.42	23	24	plus 4.3
	28	30	plus 7.1
	38	40	plus 5.2
	43	45	plus 4.6
	40	42	plus 5.0
	49	51	plus 4.1
	40	42	plus 5.0
	50	53	plus 6.0
	48	50	plus 4.1
	58	60	plus 3.4
0.34	25	26	plus 4.0
	48	50	plus 4.2
	53	54	plus 1.9
	48	50	plus 4.1
	37	39	plus 5.3
	43	45	plus 4.6

TABLE I—CONT'D

PER CENT SALINE	DROP LENGTHS, EXPRESSED IN $\frac{1}{20}$ MILLIMETERS		PER CENT CHANGE
	AT START	AFTER 24 HOURS	
0.25	35	36	plus 2.8
	54	56	plus 3.7
	32	33	plus 3.1
	35	37	plus 5.7
	40	42	plus 5.0
0.17	45	45	0.0
	46	46	0.0
	37	38	plus 2.6
	33	35	plus 3.0
	35	36	plus 2.8
0.08	37	38	plus 2.6
	43	43	0.0
	35	36	plus 2.8
	25	25	0.0
	29	30	plus 3.4
Distilled water	30	30	0.0
	48	49	plus 2.0
	49	49	0.0
	50	51	plus 2.0
	108	109	plus 0.9
	40	40	0.0
	43	43	0.0
	46	46	0.0
	24	24	0.0

intersects that curve. The result is expressed in Fig. 2. On this curve, we note the mean of the observations on the fluid from stimulated follicles, and also the mean of the nonstimulated *liquor folliculi*.

Such reasoning would lead us to think that the fluid of a follicle just ready to burst has an osmotic tension equal to a solution of NaCl of 0.83 per cent; while fluid from an unstimulated follicle is equivalent to a 0.55 per cent salt solution. We would be the first to admit that such fine-drawn conclusions are not justified by the wide limit of error

TABLE II. EXPANSION OF FOLLICLE FLUID (RABBIT) IN CAPILLARY TUBES

INJECTED RABBIT LENGTH OF DROP			UNINJECTED RABBIT LENGTH OF DROP		
START	END	PER CENT CHANGE	START	END	PER CENT CHANGE
59	66	plus 11.9	13	14	plus 7.7
22	25	plus 13.6	47	50	plus 6.4
28	32	plus 14.3	47	50	plus 6.4
50	56	plus 12.0	29	31	plus 6.9
38	42	plus 15.2	20	21	plus 5.0
35	39	plus 14.3	40	43	plus 7.5
49	53	plus 8.2	45	48	plus 6.7
70	78	plus 11.4	18	19	plus 5.6
45	50	plus 11.1	50	53	plus 6.0
68	75	plus 10.3			
10	11	plus 10.0			
44	49	plus 11.4			



in our observations. However, we are convinced that there is a very real difference in the response of the two types of follicle fluid to these experiments.

If the chloride content of blood plasma is 0.64 per cent, and the total inorganic content is 0.85 per cent, a solution such as our stimulated

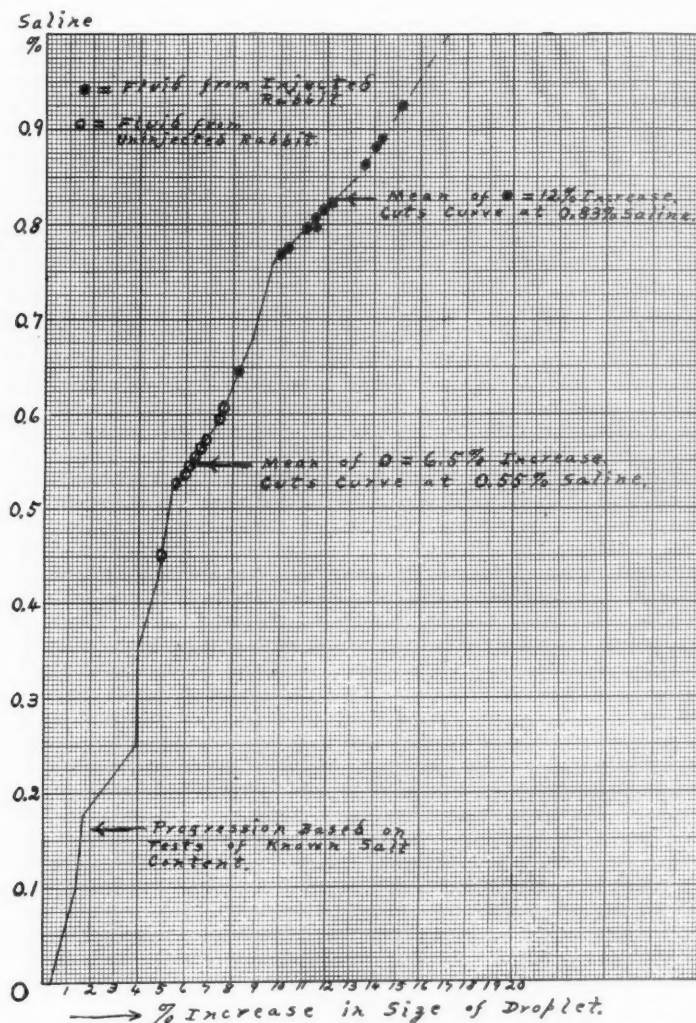


Fig. 4.—Expansion of droplets of ovarian follicle fluid (rabbit).

follicle fluid, having a content of hygroscopic substances amounting to 0.83 per cent, would be hypertonic. For not all of the inorganic plasma content is hygroscopic. For example, 0.044 is oxygen. Certainly the fluid from a nonstimulated follicle is decidedly hypotonic if its salt content is only about 0.55 per cent.

On the basis of these observations, therefore, we think there is evidence that graafian follicles enlarge and burst because the osmotic tension of the fluid is increased.

The profession is thinking much at present about the theory that some toxemias of pregnancy are caused by the great increase in the amount of circulating hormones at such times.<sup>5</sup> We are also thinking of Arnold's<sup>6</sup> teaching that edema and upset salt balance are the outstanding features in eclampsia. Can there be a hormone influence that causes an edema of a follicle in a Friedman test, and also a generalized edema of the eclamptic's body when present in excess? We hope to follow along this path with further observations in the near future.

#### SUMMARY

The phenomenon of rupture of the graafian follicles is discussed, and the theories of its mechanism are mentioned.

A method of testing the hygroscopic content of follicle fluid, based on vapor tension, is described.

#### CONCLUSIONS

Fluid from a rabbit ovarian follicle just about to rupture after the animal has been injected with urine from a pregnant woman has an osmotic tension somewhere near that of a solution of salt of 0.83 per cent.

Fluid from follicles of unstimulated rabbits has an osmotic tension equal to that of a salt solution of about 0.55 per cent.

I wish to express my gratitude to Dr. Arthur H. Bill for help and suggestions in pursuing this work.

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10515 CARNEGIE AVENUE

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Toeroek, G., and Neufeld, L.: Vitamin C Deficiency During Pregnancy, Klin. Wchnschr. 15: 417, 1936.

The authors describe a new biologic method for the determination of the amounts of vitamin C present during pregnancy. They examined 75 women during pregnancy and found that 16 or 21.3 per cent had a definite vitamin C deficiency. During the next ten days these women were given 350 mg. of ascorbic acid which resulted in a complete disappearance of the vitamin C deficiency. Since vitamin C is especially necessary to the pregnant woman during the course of the pregnancy and labor (with special reference to hemorrhage, immunity, etc.), the authors feel that vitamin C therapy is indicated in pregnancy. This is especially important during the winter months.

RALPH A. REIS.

## THE RELATIONSHIP BETWEEN INFECTED URINE AND THE ETIOLOGY OF PYELITIS IN PREGNANCY

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THE objectives of this investigation were to determine: (1) The incidence and character of bacteriuria of the bladder as compared with that of the ureter in normal antenatal and postnatal women, and (2) the etiologic significance of these to pyelitis of pregnancy.

*Theoretical and Historic Considerations.*—It is generally believed that the urine of normal pregnant women near term is frequently infected with *Bacillus coli* and occasionally with other microorganisms such as streptococci and staphylococci, without producing inflammation of the bladder or upper urinary tract. This concept, frequently referred to as the *bacilluria of pregnancy*, has been applied particularly to bladder urine, but it has also been advanced for ureteral and kidney urine as well. To explain the presence of the *Bacillus coli* in the urine of the upper tract many writers (Zangemeister, Posner, Boeda, Cathala, Bar) have postulated that this organism is excreted by the kidney under certain conditions, most prominent among which they mention pregnancy. They therefore emphasize this possibility as a means of accounting not only for the presence of microorganisms in these locations, but also for the higher incidence of pyelitis and ureteritis in the gravid woman. On the other hand, other observers express a different point of view, stating that the bladder urine, particularly near term and in the puerperium, becomes infected from the urethra, and that the ureteral urine is secondarily involved in an ascending manner, probably being regurgitated through incompetent ureterovesical valves. A third group (Kretschmer, Dudgeon, Williams, Smith, Luys, Le Fur) has been unwilling to accept either of these explanations of the route of infection and has preferred to believe that the lymph stream is primarily responsible, supposing that it brings organisms, particularly *B. coli*, from the bowel, the gallbladder, the vagina or bladder to the upper portions of the urinary tract, where they multiply and frequently attack the walls of the kidney pelvis and ureter. We are lacking in the elements of evidence necessary to establish any of these theories upon a firm basis, so that the preventive and curative treatment of urinary tract infections complicating pregnancy have necessarily been based upon empirical foundations rather than those of a more definite and specific nature. It is the purpose of this

paper to present evidence concerning the incidence of bacilluria in normal pregnancy which, we believe, tends to support the theory that the lymphatics of the bowel and pelvis transmit the *Bacillus coli* to the urinary tract in the pregnant woman, as well as to point out a few of the means which may be adapted to the antenatal care of women which will tend to reduce the incidence of pyelitis of pregnancy.

In the past there have been numerous studies of bladder urine, all of which have seemed to demonstrate beyond doubt that the urethra and bladder are often infected in late pregnancy and the puerperium, and further, that this can occur with no manifestations of cystitis or ureteritis.

Albeck (1907) made the first extensive survey, the results of which supported this point of view. Since Albeck's report, many others have studied the bladder urine and have more or less definitely verified his findings. Of such reports one should mention the following: Duncan and Seng (1928) found the urine infected in 42 per cent of their antepartum and 80 per cent of their postpartum patients; Crabtree and Prather (1930) reported a much lower incidence in antepartum women, namely 13 per cent; while in more recent reports, Harris and Herrmann (1936) found that 74 per cent of their antepartum and 94 per cent of their postpartum patients had bacilluria, and both Dodds and Baird, who studied very large numbers of women, found an incidence of infected bladder urine of 6.8 per cent.

That a bacteriuria of the bladder occurs in many antepartum women near term cannot be doubted. However, the wide disparity between the findings of Duncan and Seng, and Harris and Herrmann on the one hand, and those of Crabtree and Prather, Dodds and Baird on the other, leaves one in much doubt as to the actual frequency of its occurrence. It would seem necessary that further studies be made with the most careful technic possible before a definite conclusion may be justified.

Infections of bladder urine are of importance because of the possible extension of such infection from the bladder to the ureter and then to the kidney. Therefore, studies in which both the bladder urine and that of the upper tract are taken into consideration are of particular significance in any attempt to evaluate the etiology of upper urinary tract infections in the gravid woman. There are surprisingly few observations of this nature in the literature.

The first was that of Albeck, whose findings in 30 patients are as follows:

Thirteen patients in the first half of pregnancy:

BLADDER URINE		RIGHT URETER	LEFT URETER
Coli infection	10	3	3
Staphylococcus	2	1	1
Streptococcus	1	0	0
Sterile	0	9	9
Bladder urine infection	84%	Ureteral urine infection 23%	

Seventeen patients in the last half of pregnancy:

BLADDER URINE		RIGHT URETER	LEFT URETER
Coli infection	17	12	15
Staphylococcus	0	0	0
Streptococcus	0	0	0
Sterile	0	5	2
Bladder urine infection	100%	Ureteral urine infection 70%	

Duncan and Seng in 1928 studied 42 normal pregnant women with the following results:

	ANTEPARTUM		POSTPARTUM	
	RIGHT URETER	LEFT URETER	RIGHT URETER	LEFT URETER
W.B.C.	23.0%	9.0%	8.0%	11.0%
Pus	0.0%	2.4%	2.7%	2.7%
Coliform organisms	9.0%	9.0%	2.7%	11.0%
Cocci	50.0%	35.0%	61.0%	39.7%
No growth	56.0%	47.0%	36.0%	63.0%

The high incidence of cocci in this report leads to the inference that there may have been many contaminants. Taking only the positive *B. coli* cultures as a criterion, one may conclude that there were approximately 9 per cent of true ureteral urine infections in their antepartum and 11 per cent in the postpartum patients.

Such data, and the fact that there are no others of importance available, give the impression that the bacteriology of the upper urinary tract in pregnant women needs further study, for it is extremely difficult to account for the high incidence of 70 per cent of infected urine found by Albeck, or even 59 per cent as reported by Duncan and Seng, when it is remembered that not more than 2 per cent of pregnant or puerperal women develop clinical pyelitis. If, on the other hand, they do present an accurate bacteriologic estimate of the upper urinary tract of the pregnant woman, they should be confirmed. Therefore, an investigation of the bacterial content of bladder and ureteral urine in the normal pregnant woman has been planned and carried to completion.

#### METHOD AND APPROACH TO PROBLEM

Thirty normal gravid patients were repeatedly observed with respect to the bacterial content of the urine secured from the bladder and ureter at various stages of antenatal and puerperal periods.

In obtaining the ureteral specimens, the water cystoscope was used, the right ureter catheterized and the catheter passed well up to the ureteropelvic junction. After allowing the first ten drops of urine to escape, the tip of the catheter was flamed and five drops of urine were allowed to fall directly on an ascitic-agar slant. Several drops were then taken for microscopic examination. The agar slants were incubated and reported negative at the end of five days if no growth was present. If growth occurred, subcultures were made and the organisms classified by cultural and fermentation methods.

It was hoped that by collecting the urine directly on the agar slant rather than by transferring it from a sterile tube to a slant or to broth culture medium, it might be possible to reduce contamination to a minimal degree, as well as to obviate the possible death of organisms which might result from delayed transfer to culture media and the incubator.

The bladder cultures were made just prior to each cystoscopic examination. The bladder was catheterized with a sterile glass catheter



after the urinary meatus had been cleansed and the urine collected in a sterile test tube. The bladder urine was then examined microscopically without centrifugalization and cultures made at once in beef infusion broth.

With the above technic, 30 pregnant women have been followed in the prenatal and postnatal periods, repeated examinations being carried out on the majority of them. During the study, the right ureter was chosen for observation, as this tract possesses a marked predilection toward the development of pyelitis, and by thus studying it intensively, it was hoped that the greatest possible incidence of urinary infection might be obtained. The catheter was passed into the ureter 115 times during the pregnancies of these 30 women, with subsequent examination of the urine thus obtained by microscopic and cultural methods. Seventeen patients were catheterized three or more times, six were catheterized seven or more times, and ten on only one occasion. None of the 30 patients developed clinical pyelitis or cystitis.

Of the 115 observations thus made possible, 101 specimens of urine were negative in bacteriologic culture media; 7 proved to contain chromobacterium; 4 *Staphylococcus albus*; 1 diphtheroid; 1 lactobacillus, and only 1 *Bacillus coli*. The single positive culture for *B. coli* was obtained one month postpartum from a patient who had one subsequent postpartum and four antepartum cultures with no growth of organisms. It is interesting to note that in this instance *B. coli* was found in the bladder urine of this patient, whereas it had not been discovered previously, nor was it found in the bladder subsequently.

The same type of organism was not isolated twice from any single patient, while only four women had positive cultures on two occasions, none of the latter being on consecutive examinations. It was thought that the four positive cultures of *Staphylococcus albus* were due to contaminations. The chromobacterium and lactobacillus are definitely non-pathogenic, never having been reported as a cause of urinary tract infection, and moreover, in this study, were not found in the bladder cultures at the same time that they were isolated from the kidney urine. The diphtheroids are considered by some writers to be pathogenic. However, they have never been recovered as the sole infective organisms in pyelitis. In the one instance in which they appeared in this series, the patient had previous and subsequent negative cultures. Although the streptococcus, both aerobic and anaerobic, was found on 35 occasions in bladder urine, it was not demonstrated in any cultures of ureteral urine. One cannot explain its presence in the bladder on the basis of contamination, resulting from the technic used in collecting the specimens, for were this true, it should also have been found in the ureteral urine cultures. It is therefore assumed that like the colon bacillus the streptococcus enters the bladder by way of the urethra in the majority of instances. The

presence of streptococci in the bladder and its absence in the ureter is also taken as strong evidence against the regurgitation theory of ureteritis.

The total uncorrected incidence of positive cultures from kidney urine is therefore 12 per cent; for *B. coli* alone, it is 0.86 per cent; and for pathogenic organisms, if contaminants and nonpathogens are eliminated, it is 1.73 per cent. *B. coli* was found in the bladder urine seven times, giving an incidence of 6.08 per cent for vesical colibacilluria. Table I sets forth these findings in more complete form.

TABLE I

	ANTEPARTUM				POSTPARTUM			
	FIRST HALF		SECOND HALF		FIRST 14 DAYS		LATER	
	BLAD- DER	RIGHT URETER	BLAD- DER	RIGHT URETER	BLAD- DER	RIGHT URETER	BLAD- DER	RIGHT URETER
<i>B. coli</i>	1	0	5	0	2	0	0	1
Streptococcus	11	0	18	0	5	0	1	0
<i>Staphylococcus albus</i>	14	1	22	1	5	1	3	1
Chromobacterium	0	1	1	6	0	0	0	0
Diphtheroids	5	0	6	1	1	0	0	0
Lactobacillus	2	0	2	1	0	0	0	0
No growth	8	26	18	50	4	10	10	15
	41*	28	72*	59	17*	11	14*	17

\*More than one microorganism was recovered from individual bladder cultures on several occasions, which accounts for the discrepancy between the total numbers of bladder and ureter cultures in each group.

Thus it will be seen that the results of this investigation are in close agreement with the reports of Dodds and Baird as regards *bladder urine*, their reported incidence of *B. coli* infection being 6.8 per cent as compared with the 6.08 per cent incidence of this study. There is marked disagreement, however, with the other observers who have found an incidence of from 13 per cent to 94 per cent. It would appear that their methods were faulty or their choice of patients such as to give an excessively high number of positive cultures.

As regards infection of *ureteral urine*, on the other hand, the comparison of results is as follows:

		RIGHT URETER
Albeck	<i>B. coli</i> infection	50.00 per cent
	Total positive cultures of all organisms	51.00 per cent
Duncan and Seng	<i>B. coli</i> infection	11.00 per cent
	Total positive cultures of all organisms	50.00 per cent
Present study	<i>B. coli</i> infection	0.86 per cent
	Total positive cultures of all organisms	12.00 per cent

A perusal of these figures indicates that in the 30 women studied the incidence of infection of the ureteral urine was much less than that observed formerly in supposedly similar groups of pregnant women.

While the number of observations is too small to permit of absolute conclusions, it is sufficiently large to suggest that additional investigations may greatly modify prevailing conceptions as to the frequency of infection of the urine of the upper tract in normally pregnant women, as well as to confirm a fairly low figure for the incidence of bladder bacilluria.

Many of the patients studied developed the usual dilatation of the ureter characteristic of pregnancy, and a few of the multiparas had cystocele, so that presumably the group was a fairly representative one with respect to retardation and embarrassment of the urinary flow.

It would seem, therefore, that the conception of the normal gravid woman's urinary tract as one beset by numerous microorganisms, particularly *B. coli*, is incorrect and should be modified. Moreover, it would appear that the theory of excretion of bacteria by the kidney lacks substantiation. If this ever occurs in the normal woman, it must be a transitory phenomenon; certainly it cannot be regarded as a usual accompaniment of the pregnant state.

The regurgitation of infected urine from the bladder into the ureters was not demonstrable in any of these patients, for only once in 115 simultaneous observations of bladder and ureteral urine was the same organism recovered from both fields, although as stated above, several of the patients obviously had some degree of stasis of bladder and ureteral urine.

That urinary stasis plays a major rôle in explaining the etiology of pyelitis and ureteritis in pregnancy is unquestionable. This has impressed everyone who has made a study of this disease syndrome. However, stasis alone does not produce the disease. The portal of entry of the chief microorganism concerned, *Bacillus coli*, has not been satisfactorily clarified. From investigations such as this, it becomes more and more apparent that bacillary access into the ureter and kidney pelvis is, in all likelihood, not from the urinary tract itself in most instances, but is probably to be found in the lymph stream and then only when there is disease or stasis in other organs of the lower abdomen and pelvis which harbors the colon group of microorganisms.

From a practical point of view, these conclusions should indicate the importance of thorough elimination through the bowel, as well as the investigation of chronic appendicitis, chronic cervicitis, and chronic cystitis in the pregnant woman, as a preventive form of antenatal care to reduce the incidence of urinary tract infection due to the coliform organisms. In addition, the thorough flushing of the urinary tract by the ingestion of fluids will accomplish much in preventing these organisms from producing local inflammatory processes when they gain entry into it.

## CONCLUSIONS

1. Colon bacillus infection of the urine of normal pregnant women is not as frequent as former reports indicate.
2. The incidence of colibacilluria of the bladder was found to be 6.08 per cent, of the right ureter 0.86 per cent.
3. No evidence was found to substantiate the theory that the kidney excretes microorganisms during pregnancy.
4. No support for the regurgitation theory as to the origin of ureteritis was found.
5. Repeated catheterization of the ureter may be carried out in the pregnant woman without danger of introducing infection, if careful aseptic technic be observed.
6. The view is expressed, with some reservations, that colon bacillus infection of the urinary tract in pregnant women probably occurs by way of the pelvic and abdominal lymphatic stream with transference of microorganisms from the large bowel, etc., to the vicinity of the kidney and ureter.
7. Emphasis is placed upon the hygiene of the large bowel and urinary tract, as well as the importance of ruling out chronic infections as an essential part of prenatal care of pregnant women.

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**Wobker, Walter, and Ranft, Wolfgang:** The Treatment of Pruritus Vulvae With X-Ray, München. med. Wehnschr. 31: 1275, 1936.

Wobker and Ranft present the results obtained with roentgenization in 30 patients afflicted with primary or essential pruritus vulvae. Cure occurred in 8, improvement in 15, while 7 showed no improvement whatsoever.

C. E. PROSHEK.

## CONTRACTION RING DYSTOCIA

### AN ANALYSIS OF THIRTY-SIX CASES, WITH OBSERVATIONS ON THE USE OF ADRENALIN IN TWENTY CASES

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**D**YSTOCIA due to a contraction ring is a rather uncommon complication in labor. This article is based on 36 cases diagnosed during 14,080 deliveries on the Obstetrical Service of the Louisville City Hospital between Jan. 1, 1926, and Sept. 30, 1935, inclusive, an incidence of one in 391 labors. Only those cases in which the contraction ring was palpated by a member of either the attending or resident staff are included. Twenty cases since Jan. 1, 1931, have been treated by hypodermic injection of adrenalin; sixteen cases prior to that time were treated by other methods.

Several factors have been considered with the object of noting any common condition in all or most of our cases:

*A. Menstrual Irregularities.*—Onset, cycle and amount of flow are noted in the histories.

Normal menstrual history	25 or 70.0%
Slight irregularities	5 or 13.5%
Gross irregularities	2 or 5.5%
Not recorded	4 or 11.0%

Menstrual irregularities do not appear to play a part in the condition. Probably this may be interpreted as denoting that the contraction ring is not due to endocrine disturbance.

*B. Toxemia.*—Toxemias as revealed by elevated blood pressure seem to have no bearing on the etiology of contraction ring. In this series 6 patients had systolic pressures of 130 mm. Hg or over and of these only 3 were over 150 mm. Hg at any reading during pregnancy or labor. These 3 patients had diastolic pressures of over 90 mm. Hg, two being admitted with eclampsia.

*C. Syphilis.*—The blood Wassermann reaction was positive in 6 cases, 2 other patients who were negative at time of delivery had been treated previously; the blood Wasserman was not done in 5 cases, and was found to be negative in 23 or 66 per cent.

*D. Age.*—Harper found all patients between twenty-four and thirty-six years of age; Michael found the average age of 44 patients to be 33.4 years. In our series the youngest patient was fourteen years, the oldest forty-five years, with an average of 24.3 years. Age seems to play no part in producing a contraction ring.

*E. Parity.*—Gilliat found in his series of 14 patients that 85 per cent were primiparas. All of Hicks' 5 patients were primiparas. Michael and Harper noted the condition in equal numbers of primiparas and multiparas. White found the condition twice as common in multiparas. In our series 17 were primiparas, 19



multiparas; of the multiparas 7 were para ii. However, as the ratio of primiparas to multiparas delivered on our service is about 2:5, this may indicate that the condition is slightly more common in primiparas.

*F. Type of Pelvis.*—White and Rucker make as a differential point that retraction ring occurs in obstructed labor due to contracted pelvis or some mechanical obstruction, but that in labor complicated by the development of a contraction ring there is no disproportion between the pelvis of the mother and the presenting part of the fetus.

In our series, the diagonal conjugate was measured in 26 patients and found to be 11 cm. or more in 22 cases. In the remaining 10 cases the diagonal conjugate has been assumed to be normal in 6 patients, as they were multiparas and had had normal deliveries previously. In other words 28 patients or 78 per cent may be considered as having a normal diagonal conjugate. Four primiparas were not measured and four patients were typed as having either generally contracted or flat pelves.

*G. Length of Labor.*—The average length of the first stage of labor in primiparas is usually given as sixteen hours, in multiparas eleven hours; of the second stage in primiparas one and three-fourths hours, in multiparas three-fourths hour. In labors complicated by contraction ring both stages are prolonged. In our series Table I will illustrate.

TABLE I

	FIRST STAGE	SECOND STAGE
Primiparas	5½ hr. to 77½ hr.; av. 30.0 hr.	½ to 24 hr.; av. 4¼ hr.
Multiparas	3½ hr. to 32 hr.; av. 17.9 hr.	½ to 8 hr.; av. 3½ hr.

Falls cites lengthened labor as a factor in producing contraction ring but it may be rather that contraction ring prolongs labor.

*H. Analgesia.*—It is the custom on this service to give all patients in labor sufficient analgesia to make labor quite bearable. In this series of 36 cases (excluding 5 cases sent in by private doctors after attempts at delivery elsewhere with no records as to the analgesia), 9 received no analgesia or only light chloroform analgesia late in second stage, 7 (each a primiparturient) received Gwathmey analgesia, 6 received morphine sulphate once or more, 5 received morphine sulphate and barbiturates, 3 received barbiturates only, and 1 received morphine sulphate and scopolamine.

This amount of analgesia compares with that usually given in labor. Many patients, particularly those of the so-called "neurotic" type, have received considerably more analgesia than any of the above. The staff and nurses do not recall any case of contraction ring developing in a "neurotic" individual.

*I. Premature Rupture of Membranes.*—This condition is given as an etiologic factor by several authors although in our series it does not appear to be a constant factor as Table II shows.

TABLE II

Prematurely (2 hr. to 3 days before onset of labor)	9 cases or 25.0%
During first stage (cervix dilated 4 cm. or more)	5 cases or 14.0%
At complete dilatation of cervix	15 cases or 41.6%
Not recorded	7 cases or 19.4%

*J. Intrauterine Manipulation and Rectal Examinations.*—Some consider that contraction ring develops because of intrauterine manipulations. On this obstetric service most parturients are examined and diagnosed by rectal and abdominal

examinations only, until prepared for delivery. In the patients developing contraction ring, there was an average of 4 rectal examinations in each case and this is not out of the ordinary. Vaginal examinations were *not* done before the patient was prepared for delivery in 21 cases. In patients with slow or no progress, vaginal examinations were made. During labor one vaginal examination was done in 2 cases, 2 vaginal examinations in 3 cases and 3 or more vaginal examinations in 10 cases; but of these 10 cases, 5 patients were sent in to the hospital after attempted deliveries elsewhere. In 3 of the patients in whom vaginal examinations were done, intrauterine manipulations were performed for the insertion of Voorhees' bag, and this was done before the contraction ring was diagnosed.

Of course vaginal examinations were made frequently *after* the diagnosis of contraction ring but these cannot be considered as causative factors.

Since intrauterine manipulations or vaginal examinations were only done in 42 per cent of these cases, it does not appear that such examinations are etiologic factors.

*K. Malpresentations.*—The only constant finding which might be interpreted as an etiologic factor was malpresentation in practically all of our cases. Only one case is recorded as presenting in L.O.A.; one presentation is not recorded. Thirty-four patients (94.4 per cent) showed abnormal presentations:

LOP	13 cases or 36.0%
ROP	12 cases or 33.3%
(Cephalic presentation)	25 cases or 69.3%
Breech	5 cases or 14.0%
Transverse	4 cases or 11.0%

Obviously this may be only a concomitant condition instead of an etiologic factor, or in other words, since we do not know the cause of malpresentation the same factor may be in effect to cause both conditions.

*L. Other Conditions.*—Twenty-seven women had visited the prenatal clinic during pregnancy, and nine were first seen in labor. There were 17 white and 19 colored patients. These conditions usually obtain on this service.

#### DIAGNOSIS

The diagnosis of contraction ring was made by palpation of the ring vaginally in all our cases. It is the rule in this department to investigate the cause of delay after the cervix has been completely dilated one and one-half hours in primiparas and one hour in multiparas, and if the delay is considered due to uterine inertia to apply low forceps. In 6 cases low forceps were applied and when moderate traction did not effect delivery, further examination revealed a contraction ring around the neck of the fetus. Contraction ring was encountered in 5 cases in which version was attempted. In three cases a contraction ring was found around the neck preventing the descent of the after-coming head in breech extraction. In our last three cases on vaginal examination the cervix was found fully dilated, and hanging like a "cuff" around the head of the fetus, while the uterus continued to contract and relax rhythmically, but a thick rubbery contraction ring was found around the neck of the fetus.

Several writers do not make any differentiation between contraction and retraction rings, and in our records none is made, but on careful

perusal of the records there are some cases which suggest the presence of retraction rings found in obstructed labor. The grim picture painted by Falls was seen; "The mother is usually much exhausted, often has a degree or two of fever, and a pulse of 110 to 130. The membranes are usually ruptured and infection of the uterus may be taken for granted, especially if numerous vaginal examinations have been made, as is usually the case, and if there have been previous attempts at operative delivery." Four of our six deaths occurred in these cases.

A contraction ring may continue for an indefinite period. In one of our patients, it was found still present twenty-four hours after first being diagnosed, the uterus continuing to contract rhythmically all that time. In our last patient the ring was again palpated three hours after being diagnosed, and during that time the pains continued regularly. In only one of our patients was the ring noted to have relaxed, and the patient, two hours after being given caudal block and adrenalin, delivered spontaneously.

#### PREVENTION

Inasmuch as no common etiologic or concomitant factor has been noted, except malpresentation, any rational preventive seems lacking. Since occipitoposterior positions were found in 70 per cent of cases, correction of these positions should be attempted by external manipulations and/or favorable positions of the patient in labor. Of course, the patient should be given supportive treatment to obviate the exhaustion of long labor.

#### ACTION OF ADRENALIN

Rucker, in 1925, in researches on the action of adrenalin on the uterus found that adrenalin injected subcutaneously inhibited contractions of the uterus for from nine to thirty minutes after the injection. In 1927 he reported two cases in which he used adrenalin subcutaneously with caudal block to relax a contraction ring successfully. Since that time many cases have been reported. Rucker, in discussing the action of adrenalin on the uterus, works out the following rationale of treatment:

1. The uterus is innervated by sympathetic and parasympathetic nervous systems.
2. The sympathetic system probably acts as an inhibitor of uterine action.
3. Adrenalin, the sympatheticomimetic hormone, inhibits uterine contractions and thus, rationally, should relax a contraction ring.

(Apropos of this action of adrenalin on the uterus, might the poor contractions of the uterus in women who are much frightened in labor, be due to an excess of adrenalin in the blood resulting from fear?)

Adrenalin also relaxes a retraction ring, but this does not remove the cause of dystocia.

In our series of 36 cases, there were 16 patients treated prior to the use of adrenalin. These 16 patients were, all but one, treated by deep

surgical anesthesia, one patient, an eclamptic, being given gas oxygen anesthesia. The results are given later.

Since January, 1931, all our patients have been given adrenalin, one or more doses subcutaneously, in the treatment of contraction ring dystocia. It was found that adrenalin alone was not always sufficient to relax the ring, so that most patients were also given deep surgical anesthesia. At the present time our method of treatment of contraction ring, which has proved very satisfactory, is as follows:

#### TREATMENT

When a contraction ring has been diagnosed by palpation, the patient is given morphine sulphate, 0.016 gm. (gr.  $\frac{1}{4}$ ) subcutaneously. Ether is then given to deep surgical degree, by which time the morphine sulphate has begun to have its relaxing effect also. As soon as the patient is well under ether, adrenalin 0.5 c.c. is given subcutaneously and repeated in five minutes. After ten minutes, the contraction ring is again palpated and is found relaxed sufficiently to allow extraction of the fetus by low or midforceps, or by version and extraction. In cases in which ether is contraindicated (e.g., toxemias, upper respiratory tract infections) caudal block is used. It is advisable to be in readiness to inject pituitrin (minims iii) or ergotrate (0.2 mg.) intravenously immediately after the expulsion of the placenta to control excessive hemorrhage should this occur.

#### METHODS OF DELIVERY

There was only one spontaneous delivery in this series as noted above. All other deliveries were effected by operative means. Table III gives the methods used.

TABLE III

	DONE	UNSUCCESSFUL
Cesarean section	1	
Breech	3	
Version and extraction	16	3
Forceps on after-coming head	6	
High forceps	6	1
Midforceps	6	2
Low forceps	3	

#### RESULTS

The published figures as well as our own results mark this condition as one of the gravest obstetric complications and the prognosis for both mother and child is always grave.

Michael collected 43 cases from the literature and found a maternal mortality of 28 per cent and a fetal mortality of 59 per cent. Croft reports 2 cases with 50 per cent maternal mortality and 100 per cent fetal mortality. Hopkins had three cases with no maternal mortality. Rudolph, in a review of nearly 300 collected cases, found a maternal mortality of 15 per cent and a fetal mortality of 46 per cent. His own series of 21 cases had a maternal mortality of 9.5 per cent and a fetal mortality of 28 per cent.

In our series of 36 cases, there were six maternal deaths. Four women died shortly after delivery, three of them having ruptura uteri. The remaining two died on the ninth and tenth days postpartum of bronchopneumonia and puerperal sepsis, respectively. Since the use of adrenalin, beginning January, 1931, there have been no deaths from sepsis and two maternal deaths from ruptura uteri, one patient being admitted with uterus ruptured.

For the fetus the condition is extremely grave. The fetal mortality in our series was 64 per cent, 4 being dead in utero, giving a corrected mortality of 59.4 per cent. Prior to the use of adrenalin 3 craniotomies were done and 5 babies died of birth injuries, in 16 cases. Five babies were discharged alive and well. In the last 20 cases only one craniotomy has been done but 10 babies died of birth injuries. Eight babies were discharged alive and well.

Table IV consolidates the above figures.

TABLE IV

	TOTAL		PRIOR TO USE OF ADRENALIN		SINCE USE OF ADRENALIN	
	NO.	%	NO.	%	NO.	%
Maternal mortality	6	16.6	4	25	2	10
Maternal morbidity	10	27.7	3	19	7	35
Gross fetal mortality	23	63.8	11	69	12	60
Dead in utero	4		3		1	
Craniotomy	4		3		1	
Died of birth injury or intrauterine asphyxia	15		5		10	
Corrected fetal mortality	19	59.4	8	62	1	58
Babies discharged alive and well	13	36.1	5	31	8	40

## SUBSEQUENT DELIVERIES

It has not been possible to follow up all these patients but seven have been delivered subsequently by the service. One patient had three subsequent cesarean sections, a second patient had a placenta previa, a third had a breech delivery and a second pregnancy with a cephalic presentation three years later. In the 7 patients who returned to our service, there were thirteen subsequent pregnancies with 8 spontaneous deliveries. Contraction ring did not develop in any of these subsequent deliveries.

## COMMENT

The use of adrenalin to relax a contraction ring developing in labor has led, I believe, to decrease in the maternal mortality rate. Although the fetal mortality is still high, it is gratifying to note that fewer craniotomies were necessary on living babies, and that more babies were discharged alive and well.



In tabulating the results no attempt has been made to differentiate contraction ring dystocia from that due to obstructed labor leading to retraction ring, because no definite diagnosis was made in the histories. However, it is important to differentiate the two conditions. Although adrenalin may relax the muscles in a retraction ring, the cause of dystocia is not removed and the case is still formidable.

In dystocia due to contraction ring, adrenalin relaxes the ring and thus removes the cause. The case may terminate by spontaneous or operative delivery, depending on the condition of the patient and the judgment and skill of the accoucheur.

Although a comparison of the results before and after the use of adrenalin does not reveal spectacular improvement, yet it is the feeling of the staff on our service that such cases are now much more easily handled than previously.

#### CONCLUSIONS

1. Contraction ring should be differentiated from retraction ring developing in labor because the treatment of each depends on a correct diagnosis.

2. No common factor has been noted in all cases developing contraction ring, i.e., the etiology is still obscure.

3. Adrenalin, assisted by morphine sulphate and deep surgical ether, will relax a contraction ring.

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1525 MEDICAL ARTS BUILDING

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**Sarkar, M. N.**: Epidemic Dropsy in Pregnancy, Calcutta M. J. 29: 539, 1935.

Cases of epidemic dropsy during pregnancy are presented. This condition usually terminates the pregnancy. This unfavorable result may be attributed to a hormonal unbalance which causes vasomotor changes in the vessels of the uterus and ovary. The factor of infection is emphasized, subinvolution and damage to the heart are common.

Beri-beri and epidemic dropsy are not identical conditions. Epidemic dropsy in pregnancy may prove fatal after miscarriage. Edema of lower extremities and a brawny chocolate or coffee-like appearance and hemorrhage of the gums are typical classical signs of epidemic dropsy. Hemorrhage in the gums and in the decidua are simultaneous and are dangerous signs. Protein foods, digitalis and calcium are the routine treatment for this condition.

F. L. ADAIR AND S. A. PEARL.

## TRICHOMONAS VAGINALIS VAGINITIS\*

### INCIDENCE, DIAGNOSIS AND TREATMENT WITH SILVER PICRATE

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IT BECAME apparent following the paper of Greenhill in 1928 that many cases of *Trichomonas vaginalis* vaginitis were wrongly diagnosed or undiagnosed. Bland, Goldstein and Wenrich in 1931 showed the high incidence of this condition in pregnant women, and also that it is a factor in puerperal morbidity, so that the importance of this infestation is now well recognized.

#### INCIDENCE

During ten months a routine search was made for *Trichomonas vaginalis* in the vaginal canal of all white patients entering the Gynecologic and Prenatal Clinics of the Philadelphia General Hospital. For purposes of comparison the colored patients were likewise examined for a period of one month. Of the 532 patients who were examined in this series, 168 (31.6 per cent) were found to harbor the trichomonad in the vaginal canal. As may be seen in Table I there was only a slight difference in the incidence of infestation in the nonpregnant and pregnant groups. However, by comparison, the percentage of positive cases found in the colored patients was almost double that observed in the white patients. There was no seasonal variation of incidence. The patients examined were all above twelve years of age. In addition to the female patients studied, an examination of the prostatic secretion in 102 male patients was made, and in 4 cases (3.9 per cent) *Trichomonas vaginalis* was found. Although it was one of the original aims of this work to attempt to find an explanation for the mode of infection or re-infection of the vaginal canal with *Trichomonas vaginalis*, nothing conclusive was found in this series nor in the literature. Therefore, a discussion of the mode of infection will not be included.

#### DIAGNOSIS

The clinical picture commonly associated with trichomonas vaginitis was seen in all of the acute cases in this series. It is of interest to note that in four cases (2.4 per cent) the chief complaint of the patient was

\*Presented in part at the Scientific Exhibit of the Eighty-Seventh Annual Session of the American Medical Association, Kansas City, Mo., May 11-15, 1936.

The authors wish to express their appreciation to Dr. J. H. Clark, Pathological Laboratory, Philadelphia General Hospital, and to Dr. D. H. Wenrich, Department of Zoology, University of Pennsylvania, for their interest and assistance in this study; and to the nursing staff of the Gynecological and Prenatal Clinics for their aid in handling the patients.

lower quadrant pain which could be accounted for by no other finding in the pelvis. A similar observation was made by Goodall in 1933. In spite of the ease of diagnosis of *Trichomonas vaginalis* vaginitis from its clinical manifestations, in order to make this diagnosis positive it is necessary to see the moving organism in the fresh smear. The following method proved satisfactory for this purpose.

TABLE I. INCIDENCE OF TRICHOMONAS VAGINALIS INFESTATION

	TOTAL	WHITE	COLORED
<i>Females (vaginal smear):</i>			
Number of patients examined	532	426	106
Number of patients positive	168	117	51
Percentage positive	31.6%	27.5%	48.1%
Gynecologic patients examined	319	229	90
Gynecologic patients positive	108	65	43
Percentage positive	33.8%	28.3%	27.7%
Prenatal patients examined	213	197	16
Prenatal patients positive	60	52	8
Percentage positive	28.1%	26.4%	50.0%
<i>Males (prostatic secretion):</i>			
Number of patients examined	102	72	30
Number of patients positive	4	3	1
Percentage positive	3.9%	4.1%	3.3%

With the patient in the lithotomy position an unlubricated speculum was inserted into the vagina. Lubricants of the glycerin, oil or jelly type dehydrate the organisms, render them immobile, and thus make diagnosis uncertain. When lubrication is necessary, some of the vaginal secretion may be rubbed on the blades of the speculum, or salt solution may be used. A cotton applicator was then used to secure a small amount of the secretion from the deeper part of the vagina. The applicator was then inserted into a test tube containing 5 c.c. of modified Ringer's solution\* or normal saline and the test tube shaken to mix the vaginal secretion thoroughly with the Ringer's solution. A drop of this mixture was then placed upon a glass slide and immediately examined under the high power dry lens of the microscope. The diagnosis is positive when the moving trichomonads are seen.

While our diagnosis was always confirmed by culture this is not deemed necessary in practice since only two more positive results were obtained by culture than by direct smear. Our culture method is as follows:

1. Prepare any required number of test tubes, containing 10 c.c. of modified Ringer's solution, by sterilizing in an autoclave for twenty minutes at fifteen pounds' pressure, the tubes being closed with cotton plugs.
2. Immediately preceding inoculation of these tubes for culture, add 0.01 gm. of Loeffler's dehydrated blood serum to each tube.
3. From a test tube containing a mixture of five cubic centimeters of modified Ringer's solution and a small amount of vaginal secretion take one cubic centi-

\*Modified Ringer's solution: NaCl 6.0 gm., KCL 0.1 gm., CaCl<sub>2</sub> 0.1 gm., NaHCO<sub>3</sub> 0.1 gm., distilled water 1000 c.c. (Drbohlav).

meter and add it to the sterile tube containing modified Ringer's solution and Loeffler's blood serum.

4. Incubate at 37.5° C. for twenty-four hours.
5. Examine microscopically for presence of the organism.
6. Subculture every forty-eight to seventy-two hours.
7. Subculture into tubes containing 0.01 gm. of gastric mucin in each test tube of modified Ringer's solution and Loeffler's blood serum.

#### TREATMENT

The treatment of *Trichomonas vaginalis* vaginitis as devised by DeLee in 1920 is now known as the "wet" method and has had many modifications. Originally the treatment consisted in thoroughly scrubbing the vagina with green soap and water, under anesthesia if necessary, and then a solution of 1:1,500 mercuric bichloride was applied to the vaginal mucosa. This procedure was repeated the next day and the vagina packed with sodium bicarbonate and glycerin. After this a douche of 2 per cent sodium bicarbonate was used twice daily until the symptoms disappeared. Modifications of this method of treatment met with a certain amount of success. Due to the pain caused by the treatment and the frequency of recurrences if not followed completely, this method has gradually lost favor and at present the "dry" methods of treatment of *Trichomonas vaginalis* vaginitis are in vogue.

The use of a powder was first popularized by Gellhorn who sprayed kaolin and sodium bicarbonate with 12.5 per cent acetarsone into the vagina with a special insufflator. Kaolin, quinine sulphate, and sodium bicarbonate have also been used in the "dry" treatments. More recently the use of arsenic derivatives has met with success. The dry methods of treatment are advantageous from the point of view of both the physician and the patient. In 1931 Goodall introduced 1 per cent picric acid suppositories as a treatment for trichomonas vaginitis, and in 1936 Shelanski showed that silver picrate is the most effective silver salt for destroying trichomonas in vitro. Therefore, it was decided to use as the basic part of our treatment a powder consisting of one part of silver picrate dispersed upon ninety-nine parts of kaolin.\* To supplement this a suppository containing 2 gr. of silver picrate in a boroglyceride-gelatin base was used. The rationale of this method of treatment rests upon the fact that a combined antiseptic and drying agent (silver picrate-kaolin powder) is introduced into the vagina, and the time of action of the antiseptic agent is prolonged by periodic insertion of the suppositories. Our method of treatment was as follows:

After a positive diagnosis of trichomonas vaginitis had been made, the patient was placed in the lithotomy position and 5 gm. of silver picrate-kaolin powder was blown into the vagina by means of a special insufflator, care being taken to use only enough pressure to balloon out the vaginal walls. The patient was then given six vaginal suppositories of silver picrate, one to be used each night, and she was

\*Supplied through courtesy of John Wyeth & Brother, Inc.

instructed to return in one week. At this time a smear was taken and the vagina again was insufflated with silver picrate-kaolin powder and six more suppositories were supplied. The patients were examined for trichomonas seven and fourteen days after the original insufflation, and also at the end of each menstrual period for the next six to nine months. Cultures of the vaginal secretion for *Trichomonas vaginalis* were made at each examination.

#### RESULTS OF TREATMENT

Of the one hundred and sixty-eight patients found to harbor *Trichomonas vaginalis*, it was possible to treat and follow up 100 individuals, 62 for six months and 38 for nine months. There were three recurrences in this group, occurring at the fifteenth, eighteenth, and twenty-first week after the original treatment in three patients. Two of these were again treated and remained negative up to their last appearance at the clinic, at the seventeenth and twenty-second week following the second course of treatment. At the end of the two-week period of treatment, it was found that the discharge disappeared in 90 per cent, the itching in 94 per cent, and the burning in 96 per cent of the 100 patients, and smears and cultures were negative in 100 per cent. During the two-week period of treatment no attempt was made to treat other causes of vaginal discharge. In two cases, following insufflation of silver picrate-kaolin powder, there was a moderately intense local reaction characterized by itching, which quickly subsided. In each of these cases there was excessive alkalinity of the urine.

Although with this method of treatment the incidence of recurrence is low and the percentage of cases receiving symptomatic relief is high, it is felt that one of the chief advantages is the ease with which the procedure is carried out.

#### CONCLUSIONS

1. The incidence of *Trichomonas vaginalis* infestation among patients of the Gynecological and Prenatal Clinics of the Philadelphia General Hospital was found to be 31.6 per cent.

2. In white patients the incidence was 27.5 per cent and in colored patients 48.1 per cent.

3. *Trichomonas vaginalis* vaginitis is a clinical entity, and bilateral lower quadrant pain is an occasional symptom.

4. The mode of transmission and the reason for recurrence of the infestation are not known.

5. The use of 1 per cent silver picrate-kaolin powder in combination with silver picrate suppositories is an efficient and simple method of treatment for *Trichomonas vaginalis* vaginitis.

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## P-CARBAMINO PHENYL ARSONIC ACID IN THE TREATMENT OF TRICHOMONAS VAGINALIS VAGINITIS

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THIS report deals with the results in the treatment of *Trichomonas vaginalis* vaginitis with p-carbamino phenyl arsonic acid\* (carbarsone). For the sake of brevity, this drug will be called by its trade name.

The series consists of 21 patients who came for treatment because of a vaginitis associated with annoying leucorrhea, which was foul smelling, irritating, and caused pruritus of the vulva in 17 cases. In addition, 6 of the patients complained of chafing of the thighs. In all of these patients, the motile flagellated protozoon, the *Trichomonas vaginalis*, was found in a warm, freshly made, hanging drop of a loopful of vaginal discharge taken through a warmed and nonlubricated speculum from the posterior fornix, with the addition of a drop of warm normal saline solution. If the patient had taken a douche and no trichomonads were found, she was told to omit the douching for thirty-six hours prior to her next visit for the hanging drop examination.

In addition to examining the hanging drop, gram-stained smears were studied, primarily to determine the concomitant bacteria. These two procedures were repeated each time the patient reported for examination. Before starting treatment, the stained smear usually showed (in addition to the *Trichomonas vaginalis*) many bacteria, many pus cells, a few red blood cells, degenerated cellular debris and only seldom an occasional Döderlein bacillus. As the condition improved under therapy, the pus cells became less and less until they finally disappeared, the cellular debris disappeared and was replaced by the normal epithelial cells; large numbers of the Döderlein bacillus replaced the cocci and other organisms found previously, thus showing the reestablishment of the normal vaginal bacterial flora.

In the acute and chronic stages, a gram-positive diplococcus predominated. There were also occasionally *B. coli* and diphtheroids. No monilia were found in any patient.

The age incidence was as follows: The youngest patient was fourteen years of age and the oldest forty-nine, 13 patients, or 62 per cent, being between the ages of twenty and thirty-five.

\*P-carbamino phenyl arsonic acid is manufactured by Eli Lilly and Company under the trade name of Carbarsone.

None of the patients who were treated were virgins. The fourteen-year-old girl had had sexual relations on several occasions. All patients were still menstruating. None of them had gonorrhea concomitant with the trichomonas infection. Parity seemed to play no rôle. Eight of the patients gave the history of having been treated by other doctors previously for the same condition.

The longest duration of discharge was in an unmarried girl nineteen years of age whose discharge started shortly after the onset of her menses and who had been under medical attention for the same complaint for a period of three and one-half years. The longest duration for the discharge without previous medical care was eighteen months. This patient was twenty-six years of age, and had to wear a protective pad constantly. She was a divorcee and denied sexual relations for the last two years. The most acute case was that of the forty-nine-year-old woman, whose symptoms were only of two weeks' duration. It was impossible to make a digital examination because of the marked vaginitis.

The treatment is carried out in the following order: Each night before retiring, the patient takes a vaginal douche with a pint of lukewarm soapsuds followed by another pint of lukewarm tap water to rinse out all of the soap. She next takes a one-half pint soapsuds enema followed by another one-half pint of plain tap water. The patient is instructed to use different nozzles for vagina and rectum and keep them separated in lysol solution. After the enema, she inserts into the rectum a suppository which contains 2 gr. of carbarsone in a glycerogelatin base which should be retained all night. After inserting the rectal suppository, she instills into the vagina by means of an Asepto one-half ounce male urethral syringe 5 gr. of carbarsone with 5 gr. of sodium bicarbonate dissolved in two teaspoonfuls of lukewarm water (carbarsone is soluble only in alkaline solution). This solution is retained in the vagina all night. On the following morning she inserts one carbarsone suppository into the vagina and another one into the rectum. In the evening she repeats the described procedure but omits the vaginal soapsuds douche, and continues in this manner for six days. Acid vaginal douches as described later are taken only as is necessary to keep comfortable. In some patients, the vaginal instillation of the carbarsone-bicarbonate solution was used in the morning and then only a suppository inserted vaginally in the evening. On the seventh day, no vaginal douche is taken, and hanging drops and smears are made. At this time, if there is subjective and objective improvement, the rectal therapy is given every night for another six nights but the morning rectal suppository is omitted. The vaginal therapy is continued for another six days. On the following day, which is the fourteenth day of treatment, the hanging drop and smears are again made. At this time she is instructed to douche vaginally every morning with a pint of lukewarm water to which is added one tablespoonful of vinegar or one teaspoonful U. S. P. lactic acid, but no carbarsone. If the douche causes burning, the same amount of vinegar or lactic acid is diluted in two pints of water. During this third week, she inserts a carbarsone suppository vaginally every night before retiring, and at the same time, a carbarsone suppository rectally every other night.

After three weeks of this treatment all rectal therapy is discontinued, and the patient takes a vaginal douche every other morning and the same evening uses a vaginal suppository, until the onset of her menstruation. During her menstruation, she douches morning and evening with the vinegar or lactic acid solution, and also uses a carbarsone suppository every night before retiring. One or two days after the cessation of menstruation, she discontinues the douches and carbarsone for at least forty-eight hours, and reports for a hanging drop and smear examination.

The above treatment is started immediately after the cessation of a menstruation, so that it can be carried out uninterruptedly over a period of twenty-one days.

#### RESULTS

All patients thus treated showed absence of trichomonads and change to normal flora within two weeks. In spite of these findings, this form of treatment was continued until the end of the next menstruation to prevent a possible relapse, which is prone to recur after menstruation. The patients are instructed to return for follow-up every three months or oftener, should symptoms recur. With two exceptions, all of these patients have been found free of subjective symptoms and trichomonads after one course of treatment lasting twenty-one days.

The longest cure to date has been twenty-five months and the latest patient included in this series has been free of trichomonads for a period of three months.

The histories of the two aforementioned exceptions are as follows:

CASE 1.—Patient, aged twenty-six years, married, never pregnant, complained of marked dyspareunia and vaginitis. Trichomonads were found and treatment was instituted. All symptoms disappeared and the patient was discharged. When returning, as instructed after three months, she had her original complaints and symptoms, and on examination I again found the trichomonads and associated bacteria. I ascertained that her husband had a urethral discharge with painful urination, and that a urologist was "treating his prostate." No condom had been used. Husband denied ever having had a gonorrhea. A fresh condom specimen examined immediately after intercourse showed numerous motile trichomonads. His physician then discovered trichomonads in the prostatic secretion. We were unable to find gonococci in his secretion. Presumably, the patient had been reinfected by her husband.

CASE 2.—Patient, aged twenty-nine years, married, came for a severe leucorrhea which had been present off and on "for some time." Examination of vaginal secretion established the diagnosis of *Trichomonas vaginalis* vaginitis. Treatment was instituted and after three weeks she was pronounced free of the disease. Three months later, she was still free of symptoms, no trichomonads were found, and the vaginal flora was normal. She had no intercourse for three months since treatment was stopped. Two months later, she again reported to me because of a vaginitis, and *Trichomonas vaginalis* was found. Sexual relations had been resumed after her last visit. A fresh condom specimen revealed the presence of trichomonads; however, no trichomonads were found in the husband's prostatic secretion.

These two cases were the only failures out of 21 patients treated with carbarsone for *Trichomonas vaginalis* vaginitis; and only one deduction can be made in these two failures, namely, the husband also carried trichomonads and reinfected the wife during coitus.

Patients must be watched for toxic symptoms of carbarsone poisoning during the treatment (optic and renal changes). If a pelvic disorder exists an effort is made to correct it. Patients are impressed with the importance of active treatment also during their menstruation. At the same time they are told the proper after-care following a bowel evacuation, being careful not to spread the fecal material toward the vagina.

Carbarsone has been used by a number of observers for the treatment of intestinal amebiasis. Gabaldon has used it experimentally on *Trichomonas hominis* in vitro. He found that a concentration of 0.3 per cent carbarsone was always lethal in less than seventy-two hours, and when present in sublethal concentrations the reproductive rate of the flagellates is reduced. Gospe reports using carbarsone successfully in 51 patients suffering from *Trichomonas vaginalis* vaginitis.

When given orally, there is always the danger of toxic effects. The following reports of toxic symptoms following its oral use have appeared:

Epstein has reported a death following the oral ingestion of a total of 5 gm. during a ten-day interval, given for the treatment of a nonspecific dysentery of long standing. Anderson and Reed, and Smithies report untoward effects following its use orally, with recovery of the patients upon the discontinuance of the drug. The principal toxic symptoms of carbarsone poisoning as reported were: icterus, large liver, exfoliative dermatitis, swollen ankles and wrists, photophobia, faulty vision and gastric distress. The optic findings described have been papillitis and retinal edema. Casts are found in the urine.

Although in my series of cases no toxic manifestations followed its application by rectum and vagina, I feel that patients must be watched most carefully, though I have been unable to find any report of toxic symptoms following the vaginal use of this drug.

#### SUMMARY

1. A report is made of 21 cases of *Trichomonas vaginalis* vaginitis treated with carbarsone.
2. In this series, there were two recurrences, which probably represent reinfections from the husband.
3. Carbarsone administered in the manner here described caused no toxic symptoms. Nevertheless, the patients should be watched closely because of the large doses of the drug used.
4. The importance of treatment also during menstruation, and the examination of the male especially in instances of seeming recurrence are stressed.
5. The treatment of the rectum is stressed because of the possibility of its being a source of infection.
6. The treatment is carried out entirely by the patient, and thus avoids all forms of office treatment, which is generally painful at this time.

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## EVALUATION OF THE PRACTICAL USE OF THE ASCHHEIM-ZONDEK PREGNANCY TEST

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THE increasing use of the Aschheim-Zondek test for pregnancy has led us to determine, so far as possible, just what can be learned from this test. To this end, with the cooperation of the physicians involved, we have checked our results against the subsequent clinical history, when available, of those patients for whom we have made the test. A summary of the 702 cases we have been able to follow, out of over 1,100 tests, is given in Table I. In studying these data it should be kept in mind that we do not run this test routinely on all patients, but only at the request of the physician. This means that few of the average normal cases are included, and that our percentage of complicated cases, and probable errors, runs higher than in most similar studies.

It should also be noted that we have employed this test in a strictly utilitarian manner. We have used only one animal for each determination, for economic reasons, and while we have urgently advocated that only first voided morning specimens be submitted, when such were not available we have accepted others. Our percentages should not, therefore, be considered as optimal for this test. We employ immature female rats twenty-four to thirty-five days old. No preservative is used in the urine, although specimens are kept in the refrigerator. Heavy sediments, when present, are filtered off. Two cubic centimeters of urine are injected either subcutaneously or intraperitoneally each day for five successive days, and the animal is sacrificed on the sixth. With rare exceptions the results are determined by macroscopic examination. A hemorrhagic condition or corpora lutea is taken as indicative of pregnancy. Ripe, mature follicles, as such, are not considered as a positive test, but are listed as prolan A reactions.

From Table I we learn that 90.7 per cent of the tests, 327 positive and 310 negative, were confirmed by subsequent clinical findings. There were 17 false positives and 48 false negatives. Much, however, may be learned from these apparent failures. In Table II we have classified the false negatives according to their clinical histories. Of the 48, we find 17 suffered spontaneous abortion some time shortly after the test had been made. Four others gave definite prolan A reactions. Of these, one bled for nine weeks, then recovered and went to term; after the



bleeding had been stopped the Aschheim-Zondek test became positive. A second miscarried at six months, and while the remaining two were carried to delivery, they were beyond doubt threatened with abortion when the test was made. This would indicate that these failures are

TABLE I. DISTRIBUTION OF ASCHHEIM-ZONDEK RESULTS

	NO.	PER CENT OF TOTAL
Positive	327	90.75
Negative	310	
False positive tests	17	2.42
False negative tests	48	6.83
Total run	702	100.00

TABLE II. CLASSIFICATION OF FALSE NEGATIVES

	NO.	PER CENT OF TOTAL
Spontaneous abortion	17	43.7
Prolan A reaction (threatened abortion)	4	
Early tests (under 40 days)	13*	27.1*
Dilute specimen	1	2.1
Ovarian cyst	3*	6.3*
Unexplained	12	25.0
Actual total	48	100.00

\*One specimen appears in two groups.

not due to the method, but rather to some failure of the hormone itself, the presence of prolan A suggesting that the usual menstrual sequence was in progress. A negative Aschheim-Zondek report, in conflict with clinical evidence, may then be taken as evidence of a threatened abortion, and the patient treated accordingly.

In 13 of our failures the specimens were taken before the fortieth day of the pregnancy, as determined by the delivery date. The earliest positive test was obtained at three weeks. Between the twenty-first and the fortieth day we have had 25 determinations, 12 positive and 13 false negatives. We conclude from this that negative reports made on specimens collected less than six weeks from the last menstrual period are not reliable, and, unless supported by definite clinical evidence, should be repeated.

Three of the false negative cases were complicated by ovarian cysts. One of these upon removal was diagnosed as a papilliferous adenocystoma. The second disappeared, apparently as a result of the examination. The third was not removed. We also had one false positive with an ovarian cyst, and four correctly reported as not pregnant. One of these latter was a papillary adenoma. No positives were reported as having this complication. The fact that correct negative results may be found does not prove that such cysts do not complicate, and possibly invalidate, the results when the patient is actually pregnant.

The concentration of the specimen, and therefore of the hormone, is very important. One of our negative failures was very dilute, and

should not have been used. This may also account for some of our other 12 failures, where no complicating factors could be learned from the histories. We do not believe there is any direct relation between the specific gravity of the urine and the concentration of the hormone, but we do feel that a high specific gravity, unless from a diabetic, usually coincides with satisfactory hormone content. Unfortunately we have not recorded the specific gravities in this series, so cannot give the relation of failures to dilute urines.

In Table III we have given a similar classification of the false positives. The first was not an error of the test, since we later learned the patient had been taking antuitrin-S; after discontinuation of the drug the test became negative. We make no claim that pelvic inflammatory

TABLE III. CLASSIFICATION OF FALSE POSITIVES

	NO.	PER CENT OF TOTAL
History of taking antuitrin-S	1	5.88
Pelvic inflammatory diseases	3	17.65
Carcinoma of the liver	1	5.88
Cardiac lesions and high blood pressure	1	5.88
Menstrual disorders	6	35.30
Ovarian cyst	1	5.88
Menopause	1	5.88
Unexplained	3	17.65
Total	17	100.00

diseases cause false positives, but we did find that complicating condition in the histories of 3 out of the 17 false positives we obtained. The same is true regarding the carcinoma of the liver and the cardiac lesion case, although the latter, with a history of 8 miscarriages, might easily have suffered a ninth, unrecognized. The menstrual disorders offer grounds for doubt. In at least 3 of the 6 cases the obstetrician felt that the evidence pointed to an abortion having been performed, but lacked actual proof. Also a spontaneous abortion might easily pass unrecognized. Lacking evidence, however, we must record these as false positives. For this reason patients who, failing to menstruate, request a pregnancy test, then, after receiving a positive report, have menstruation reestablished, offer difficulties of classification.

Menopause is usually supposed to invalidate the test. We had one false positive from such a patient, but 7 others also in that condition gave correct negatives. The cyst has already been discussed, which leaves 3 false positives with no explanation. In these instances the use of only one rat may account for our difficulties. We have, however, recorded 18 cases where 2 or more animals were used in successive tests. In 15 of these cases, 2 positives, 9 negatives, and 4 false negatives, the report was unchanged. In two of the false negatives, where the patient was obviously pregnant, 3 rats each were used, all reported negative.

In the 3 cases where the second animal did give a different result, there was very definite clinical evidence of a change in the condition of the patient.

We are now investigating the hypothesis that continued negative results from a pregnant woman who goes to term and delivers a normal child, may possibly be associated with nitrogen retention. If the hormone is of a protein nature, and is secreted slowly, might it not also suffer retention from a slightly impaired kidney? This would account for negative results from even concentrated urines.

In the operation of the test certain difficulties are frequently encountered. Many types of medication interfere, usually killing the test animals. Quinine and arsenic are particularly bad in this respect. Only good healthy animals should be used. Intraperitoneal injections are tolerated better by the rat than subcutaneous. Specimens should be used fresh, although if kept cold they can be used as long as a week after collection. Foul-smelling urines usually prove fatal to the animals. With proper precautions, and employing the suggested restrictions, the success of this method may be raised considerably above the figure given in our tables.

#### SUMMARY AND CONCLUSIONS

Negative results from Aschheim-Zondek pregnancy tests run within the first six weeks of the pregnancy are unreliable. Positive results may be accepted.

Negative results after the first six weeks, in conflict with clinical findings, may indicate threatened abortion, particularly if the test gives a prolan A type of reaction.

Ovarian cysts complicate the situation and apparently tend to interfere with the test.

Inflammation in the region of the pelvis is frequently associated with false positive reactions.

Data obtained during menstrual disorders are difficult to classify, since unreported abortions may be recorded as false positives.

Taking into account the above-mentioned conditions, the reaction gives a very reliable test for pregnancy. As run, we had an uncorrected error of about 9 per cent.

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Lévy, S.: *Presentation of a Speculum Permeable to the X-Ray*, Bull. Soc. d'obst. et de gynéc. 25: 442, 1936.

The author describes a new speculum made of aluminum which can be used for hysterosalpingography. This speculum is not visible in x-ray pictures and does not interfere with shadows of the cervix and the isthmus of the uterus.

J. P. GREENHILL.

## A MODIFICATION OF THE VISSCHER-BOWMAN PREGNANCY TEST, WITH A REPORT ON 513 OBSERVATIONS

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C DOLFF reported in 1936 that the Visscher-Bowman pregnancy test was 95 per cent correct on occasions in which it was used to diagnose normal pregnancies, and also in 82 per cent of cases of ectopic pregnancy and miscarriage.

The Visscher-Bowman pregnancy test is purely chemical, the reaction depending on the presence or absence of anterior pituitary hormones in the urine. It is performed as follows: To 1 c.c. of urine are added one drop of 1 per cent hydrogen peroxide, 5 drops of aqueous methyl cyanide solution, and 5 drops of phenylhydrazine hydrochloride solution, and 5 drops of concentrated hydrochloric acid; the mixture is heated for twenty-five minutes in a water-bath. The test is positive if a reddish brown flocculent precipitant is observed; if the color remains straw yellow and the deposit is powdery or absent, it is negative.

From the urine of 54 proved pregnant women, Dolff's series yielded a positive result in 51 cases, or 96 per cent. In 18 cases of early pregnancy the test in his hands was accurately diagnostic except for one false positive. Dolff believes that the source of error is a high concentration of catabolic reducing substance in some specimens of urine, and with these eliminated the percentage of accuracy of the test will increase.

### AUTHOR'S SERIES

This series consists of 513 cases, 420 of which were sent to me by a staff member from his private practice. They were numbered, and I never saw the patients.

There were 79 specimens obtained from patients in the hospital and out-patient department. Each set of specimens was run with a control tube which contained urine of a nonpregnant female as confirmed by the Aschheim-Zondek test. In the series, 15 specimens were checked by the Aschheim-Zondek test. One specimen was from a patient with suspected teratoma of the testicle; one was from a woman who had an ovarian tumor, the nature of which was not determined as the patient refused operation; 10 specimens were from patients with incomplete abortions, and two specimens were from women with dead fetuses. Two specimens were from patients with suspected ectopic pregnancy. It was found that by using 6 drops of each of the reagents and heating the specimens in boiling water forty-five minutes a better and more easily read result was obtained. If one drop of concentrated hydrochloric acid is added to the 1 per cent solution of hydrogen peroxide when the solution is made up, it will retain its strength for a week to ten days, thus obviating the necessity of making up a fresh solution so often. This was the procedure used in each of the cases of this series.

The earliest positive test obtained was in patients who were two weeks past due in menstruating. Three such cases appear in this series. Twelve women four weeks

pregnant gave positive reactions. Two women who were five weeks, and 17 who were six and eight weeks pregnant gave positive results, as did, also, 4 patients who were ten weeks pregnant.

Of 15 cases checked by the Aschheim-Zondek test, there were 8 positive, 4 negative, 2 false positive reactions, and 1 false negative, an accuracy of 80 per cent. The series is very small, and no conclusions should be drawn from it.

Of the total series of 513 cases there were 40 cases in which the test was in error, or gave a false positive or negative reaction, the percentage of error being 7.7 per cent with 92.3 per cent correct results. Twenty of these 40 cases were false positive reactions, and 20 were false negative when the patients were known to be from 4.5 to 9 months pregnant. This is explained on the basis that the amount of hormone in those particular specimens of urine was not sufficient to cause a recognizable positive reaction. One case gave a doubtful reaction, and as the patient has not returned, no specimen or examination has been checked. The false positive reactions are supposed to be due to increased catabolic producing substances in the urine of these cases.

#### DISCUSSION

While the test is cheaper, simpler, and requires less time to perform than the Aschheim-Zondek test, it requires considerable experience in learning to differentiate the various precipitates obtained. It is often difficult to differentiate between a flocculent and powdery precipitate, especially when the quantity is very small. In such cases, it was found that the convex reflecting mirror of a microscope was of great assistance. By holding the test tube over the mirror at an angle of 45 degrees and looking into the mirror, it often became a simple matter to differentiate the precipitates. It was also discovered that by allowing the tubes to remain in a rack undisturbed for several hours the reddish brown flocculent precipitate was observed in specimens that were at first classed as doubtful.

In two women six months pregnant, whose fetuses had been dead about a week, the reactions were negative in one and positive in the other. In the case that gave the negative reaction, it was learned at delivery that there had been a premature separation of the placenta, and it was thought that the secretion of the hormone was dependent upon the intactness of the placenta to the uterine wall.

In the ten cases of incomplete abortion, it was found that 8 gave a positive reaction and 2 a negative one. It was thought that in those cases that gave a positive reaction some placental tissue was living and secreting enough hormone to precipitate this reaction. In those which gave a negative result and yet the patients presented symptoms (uterine bleeding, passage of clots, and pieces of tissue), and in whom retained products of conception were obtained by dilatation and curettage, it was believed that no placental tissue was actually living and secreting the hormone, or at least, in quantity sufficient to produce a positive result.

Of the two patients with suspected ectopic pregnancy upon whom the test was run, both were positive. At operation, however, no ectopic or



uterine pregnancy was found; therefore, they are classified as false positive reactions, due, supposedly, to increased catabolic reducing substances in the urine of these patients.

## SUMMARY

Total number of tests performed	513
Total number of tests in error	40
Total number of false positive reactions obtained	20
Total number of false negative reactions obtained	20
Total number of doubtful reactions obtained	1
Total number of dead fetuses with subsequent abortions, one positive and one negative result	2
Total number of suspected ectopic pregnancies, both gave a false positive reaction	2
Total number of incomplete abortions	10
Total number giving positive reaction	8
Total number giving negative reaction	2
Total number of tests checked by the A-Z test	15
Total number of tests checked by A-Z which gave a positive reaction	8
Total number of tests checked by A-Z which gave a negative reaction	4
Total number of cases checked by A-Z which gave a false positive reaction	2
Total number of cases checked by A-Z which gave a false negative reaction	1
In 15 cases checked by the A-Z test, percentage of error	20
Correct results	80
Total number of cases of early diagnosis of pregnancy	38
Total number of patients 2 weeks pregnant with a positive result	3
Total number patients 4 weeks pregnant with positive test	12
Total number patients 5 weeks pregnant with positive test	2
Total number patients 6 to 8 weeks pregnant with positive test	17
Percentage of error for entire series	7.7
Percentage of correct results for entire series	92.3

## CONCLUSIONS

1. The Visscher-Bowman pregnancy test in the total series gave 92.3 per cent correct results, and in 15 cases checked by the Aschheim-Zondek test, 80 per cent correct results.

2. It is a cheaper, easier, and quicker test than the Aschheim-Zondek and can easily be done in one's office. It is not as valuable, however, to one inexperienced in differentiating the various precipitates as C. Dolff would lead us to believe in his paper. The test requires a great deal of practice before very much accurate dependence can be placed in one's interpretation of his results. In the hands of the experienced observer it is just about as early a diagnostic test as the Aschheim-Zondek, particularly when the first voided morning specimen is used.

3. The test may be negative in cases of advanced pregnancy with a dead fetus if there is a placental separation large enough to prevent secretion of the hormone in quantities large enough to cause a positive result. This may also be the case in incomplete abortion, even though dilatation and curettage will reveal retained products of conception.

4. There were not sufficient cases of ectopic pregnancy in this series to warrant any conclusions as to the accuracy of the test in this condition.

5. In some cases of advanced pregnancy the test will be negative. This is explained by the fact that there is more hormone in some specimens of urine than in others. Had all the specimens been morning specimens, in which it is recognized that the concentration of the various hormones is greater, some of these false negative reactions would have been eliminated.

6. While this test is not as accurate as the Aschheim-Zondek, due to the false positive and negative reactions, it is to all practical purposes a fairly accurate test for those who cannot afford the costs of the Aschheim-Zondek test, or who have not the time or facilities for doing it in order to make an early or differential diagnosis of pregnancy.

7. This is only a preliminary report.

I am greatly indebted and wish to express my appreciation to Drs. A. J. Kilpatrick and J. W. Thurmond and to their secretary, Miss Schaufele, for their assistance in furnishing specimens for this work.

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## AN ANALYSIS OF 12 CASES OF SPONTANEOUS RUPTURE OF THE PREGNANT UTERUS

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THE ever increasing use of cesarean section as a method of delivery has brought to the foreground the possibility of the more frequent occurrence of one of its most serious complications in future pregnancies, namely, spontaneous rupture of the uterus.

#### FREQUENCY

During the period from 1914 to 1934 inclusive, there occurred twelve instances of spontaneous rupture of the pregnant uterus in the Woman's Hospital Obstetrical Service of 21,594 cases, an incidence of one in 1,800 deliveries or 0.055 per cent.

Reports in the literature vary from one rupture in 255 deliveries in a Moscow maternity<sup>2</sup> to one in 27,793 in Bombay.<sup>4</sup> In 1927 Davis,<sup>3</sup> in a thirty-six-year study of 147,625 confinements at the New York Lying-In Hospital, found one rupture in 810 cases. He quotes Williams finding one to 500, DeLee one to 2,114 and Craigin one to 1,333. McNeile and McBurney<sup>8</sup> found one rupture in 578 deliveries at the Los Angeles County General Hospital in a service of 17,350 cases from Jan. 1, 1923, to March 31, 1934. Bogdanowa<sup>2</sup> reviews the findings in some European clinics: Berlin (Koblanca) one to 462; Koenigsberg (Sachs) one to 577 cases from 1919

to 1929; Vienna, one to 2,000 for the last seven years and another Moscow clinic, one to 961 in a fifteen-year period from 1887 to 1902. Maljawnski<sup>7</sup> finds one rupture in 1,273 cases during 1931 and 1932. In a personal communication two general hospitals in Brooklyn were found to have an incidence of one rupture to 1,075 cases<sup>5</sup> and the other<sup>10</sup> one to 1,582 during the last fifteen years.

There were 736 cesarean sections done at the Woman's Hospital, and in three, subsequent ruptures of the uterus took place, an incidence of one in 245 cases or 0.41 per cent. All of the cases here reported had a classical cesarean section.

#### CASE REPORTS

CASE 1.—M. S., thirty-two years old, gravida v, had an ample pelvis. In the four previous pregnancies, a placenta previa with delivery at the sixth month in the first, ten years ago; the second, eight years ago, was a premature seven months' baby, which lived; the third was a full-term normal baby; the fourth, two and one-half years ago, was induced at thirty-eight weeks because of high blood pressure, with a living baby. Five years before the present pregnancy a plastic operation and an appendicectomy were done. During the present pregnancy the patient developed a toxemia, and labor was induced ten days before time. She had indefinite labor pains for twenty-four hours. Vaginal examination disclosed a 9 cm. dilatation of the cervix through which membranes and a loop of cord protruded; presentation transverse. A marginal placenta previa could be palpated on the right side. Both feet were grasped and pulled through the cervix into the midvagina. With a contraction of the uterus, the baby, weighing 8 pounds, was born to the umbilicus and then slowly and easily extracted. The placenta was easily extracted manually. Inserting the hand into the uterus, the operator found that the cervix had split in the right posterolateral position, the tear extending through the vault of the vagina into the broad ligament and the lower uterine segment for 4 cm., a complete rupture. Uterus and vagina packed. Immediate supravaginal hysterectomy done and the patient recovered.

CASE 2.—S. S., twenty-seven years old, primigravida, ample pelvis. Myomectomy two years previously. At term, after an eight-and-one-half-hour labor, there was delivery of a six-pound-eleven-ounce baby by breech extraction; placenta by modified Credé. With only a small blood loss, the patient was returned to bed in poor condition; pulse 140, very weak; skin cold and clammy. She complained of pain in the left chest. Pulse, two hours after delivery, went to 160 and became weaker. Since her condition did not improve, laparotomy was performed eight hours after delivery. At the summit of the fundus and running from before backward, there was a rent one and three-quarter inches long. Supravaginal hysterectomy and recovery.

CASE 3.—F. B., aged thirty-one years, gravida ii, ample pelvis. Previous normal pregnancy six years ago; position R.O.P. After twenty-one hours of strong pains, there was no progress beyond engagement of the head at the pelvic brim. Therefore, version was performed and the child extracted easily as far as the head. Forceps slipped off because of hydrocephalus; basiotribe of Tarnier was used and the head was extracted easily. No shock. Baby weighed six pounds, seven ounces. Vaginal examination detected a rent in the uterus on the left side, beginning at the cervix and running up to the fundus with a ragged perforation at the base of the broad ligament admitting three fingers. Temporary packing was followed by supravaginal hysterectomy. Recovery was complicated by postoperative pneumonia.

CASE 4.—S. J., aged twenty-four years, gravida ii, ample pelvis; previous pregnancy was terminated by breech extraction of a seven-pound-six-ounce baby, four

years previously. When four weeks overdue, patient went into labor spontaneously. Position R.O.A. After twenty-two hours of irregular labor pains, the cervix was found fully dilated, the membranes ruptured, considerable meconium and 30 cm. of pulsating prolapsed umbilical cord; head of large baby at pelvic brim not engaged. Easy internal podalic version performed on a nine-pound baby in good condition. Exploration discovered a rent in the lower uterine segment just posterior to the left broad ligament which passed through the entire musculature and peritoneum. Immediate complete hysterectomy; recovery.

CASE 5.—M. S., aged thirty-five years, primigravida, ample pelvis. Labor spontaneous at thirty-eight weeks, L.O.P. with early spontaneous rupture of membranes. After thirty-two hours of labor, the head was at the brim but not engaged; fetal heart failing. Vaginal examination showed the cervix to be fully dilated. Forceps were applied but no progress made. It was decided to do a version. When the hand was introduced now, there was a loop of cord posterior to the head, not pulsating; passing the hand alongside of the head, a rent was found in the lower segment of the uterus on the left side which extended 6 cm. up to a contraction ring partially closed around the child's neck. With great difficulty, version was accomplished. Since there was no bleeding from the tear, the uterus, lower uterine segment and cervix were packed with iodoform gauze. Condition became gradually poorer because of shock, and death occurred in thirty-six hours. No signs of hemorrhage. Cause of death not definitely known.

CASE 6.—J. R., thirty-year-old primigravida, with ample pelvis. Myoma found during prenatal care. Labor spontaneous at term with a breech presentation; membranes ruptured two hours later. After forty hours of moderate pains, it was discovered that the fetal heart was no longer heard and the cervix was not fully dilated. A No. 5 bag was introduced into the cervix. After twelve hours, this came out, and examination revealed the right foot presenting and a contraction ring in the lower uterine segment not throughout the entire circumference of the uterus but more on the left side. Difficult extraction was performed. The woman's pulse immediately became rapid. Placenta delivered manually. Examination showed a rent in the uterus three inches long, beginning on the left side of the vagina and extending into the broad ligament and up into the cervix. Hysterectomy was performed immediately. Three weeks in the hospital; recovery.

CASE 7.—E. T., primigravida. Five weeks pregnant. No history given. At operation, the peritoneal cavity was found filled with free blood and the left horn of the uterus had a tear in it 1 cm. in length. Rent was sutured. Pathologic examination demonstrated a 1.5 cm. fetus and blood clots. Recovery.

CASE 8.—L. A., twenty-eight years old, gravida ii, one miscarriage, now at term with a mildly contracted pelvis, probably of the flat variety. Went into labor spontaneously, and after twenty-six hours of strong pains at home, her physician tried to deliver her. Forceps were applied unsuccessfully. She was brought to the hospital. A persistent occiput posterior was found and delivery was performed by craniotomy on a nine-pound baby. An incomplete rupture of the uterus being found (site not stated), hysterectomy was performed. Recovery.

CASE 9.—M. R., thirty years of age. One child three years previously by difficult forceps delivery; now four and one-half months pregnant. During present pregnancy, had had almost daily moderate vaginal bleeding with no pain. On the morning of admission, the patient bled painlessly and profusely and her doctor gave her chloroform and "operated upon her." Upon admission, the cervix was found to be lacerated and an incomplete tear in the lower uterine segment on the right side involving the broad ligament was found. Anterior colpotomy and suture were performed. Recovery.

CASE 10.—S. F., thirty-five years old, mild funnel pelvis. Her six previous pregnancies never advanced farther than the fourth month. She had been operated upon in Munich (date unknown). A myoma the size of an English walnut was removed from the right horn of a bicornuate uterus; the other horn was atrophic and removed at the same operation together with the left tube and ovary. A classical cesarean section was done at term high in the anterior wall with the delivery of a six-pound living baby. The scar where the fibroid had been removed could not be found. She was now in good health with no symptoms, two weeks postterm, not in labor, and thirteen months after her previous cesarean operation. As the abdomen for this elective cesarean section was opened, there was noted an aperture about 3 cm. in diameter through the anterior uterine wall. The membranes protruded but there was no bleeding. The opening was extended and a five-pound-five-ounce baby was delivered; although the child cried, it subsequently died. The uterine muscle was sutured, the remaining tube sterilized, and the patient recovered.

CASE 11.—C. G., aged twenty-eight years, just minor pelvis. Gravida iii, one stillborn and a classical cesarean section eighteen months previously for disproportion (nine-pound baby). Now at term. She was in labor at home for twenty-four hours. Upon admission, the cervix was one finger dilated, fetus in transverse position, no pains, pulse 108, and patient was not thought to be in labor. Four hours later, patient began to complain of tenderness over the fundus; pulse was 140. No signs of shock or collapse. At laparotomy, the placenta and clots presented in the wound and were extracted; the child, weighing 8 pounds, was dead and lying free in the abdominal cavity. The uterus showed a complete rupture along the line of the old cesarean scar. Uterine rent sewed and patient sterilized. Recovery.

CASE 12.—C. H., thirty-five years old, gravida ii. Had a previous classical cesarean section whose indication and time were unknown. Went into labor spontaneously at thirty-six weeks' gestation. After sixteen hours of ineffectual pains, a No. 1 bag was inserted into the cervix and six hours later the patient got very weak, vomited, pulse 140 and imperceptible. Laparotomy revealed a great amount of clotted blood; the uterus was ruptured wide open and the baby and placenta were free in the abdominal cavity. Fetus dead. Uterus sutured. Patient developed pneumonia, cellulitis, and phlebitis but finally recovered.

#### ANALYSIS OF WOMAN'S HOSPITAL CASES

The cases to be analyzed fell into three groups: (A) Noncesarean section cases, 9; (B) all cases, 12; (C) previous cesarean section cases, 3.

##### A. Noncesarean Section Cases (9).

TABLE I. THE LABOR

	AVERAGE	RANGE
Hours in labor	30 hours	8½ to 52 hours
Duration of second stage	2 hours and 40 minutes	1 to 10 hours
Duration of third stage	28½ min.	3 to 90 minutes

This shows that the labors were longer than average but only moderately so. The membranes were ruptured artificially in one case and accidentally or spontaneously in five. The time of rupture was difficult to determine in some cases but in four of six, rupture occurred during the first stage.

*Method of Placental Delivery.*—In two cases manual extraction was done; in two, a modified Credé expression; in one, normal; in one, *too early for placenta*; in two, not stated. Thus of five cases only one was delivered normally.



Version and breech extraction were the usual mode of delivery preceding rupture of the uterus.

Where condition of the cervix before delivery was known it was found that in two of seven cases, or 18.6 per cent, this only partially dilated.

TABLE II. METHOD OF DELIVERY (9 NONCESAREAN SECTION CASES)

	NO.
Version and breech extraction	6
Craniotomy	1
Five weeks' gestation	1
Not stated	1

TABLE III. PRESENTATION AND POSITION IN NONCESAREAN SECTION CASES

	NO.
Transverse	1
Breech	2
Occiput posterior	3
Too early pregnancy	1
Not stated	1

TABLE IV. COMPLICATIONS

	NO.
Placenta previa	1
Prolapsed cord	3
Bandl's ring	2
Antepartum bleeding	1
Persistent occiput posterior	3
Hydrocephalus or edema of meninges	2
Dry uterus from early rupture of membranes	2
Myoma	1

#### B. All Cases (12).

There were only two of eleven cases without some complication of presentation.

The ages of patients ranged from twenty-four years in the youngest to thirty-five years in the eldest, with an average of thirty years of age.

The weights of the babies varied from 3¼ pounds (1,470 gm.) in the smallest to 9 pounds (4,080 gm.) in the largest with an average of 7 pounds (3,180 gm.). Big babies were not a factor in this series.

TABLE V. PREVIOUS OPERATIONS—ALL CASES (12)

	NO.
None	5
Cesarean sections	3
Plastic and appendicectomy	1
Myomectomy	2
Appendicectomy	1
Amputation of atrophic horn of uterus	1

There were 41.7 per cent of the patients who had no previous operative procedure. If previous cesarean sections are excluded, four of nine patients, or 44.4 per cent, were operated upon previously.

Rupture of the uterus occurred five times in patients pregnant for the first time and seven times in multiparas (58.3 per cent).

Six of seven patients previously pregnant had operative deliveries. One-half of these were cesarean sections.

The pelvis was ample in 66.6 per cent of the cases: where contraction was present, it was of the justominor or mild funnel type. In only one case was there a toxemia of pregnancy.

TABLE VI. PREVIOUS OPERATIVE OBSTETRIC DELIVERIES, ALL CASES (12)

	NO.
Cesarean section	3
Breech extraction	1
Placenta previa with induction	1
Forceps	1
None (5 are primigravidas)	6

Of the 12 cases of rupture, 9 were within two weeks of term. Among the other 3, one was four weeks past term and the other 2 were early gestation.

C. *Previous Cesarean Section Cases.*

The three previous cesarean section patients all had the classical type of operation; one eleven years previously for a bicornuate malformed uterus, another two years previously for disproportion and in the third there was no information on these points. The duration of labor in our three cases was twenty-eight hours, twenty-six hours, and none. No case was induced and one patient was not in labor. In two patients, the rupture was discovered at operation; all three patients were delivered by laparotomy. Abnormal presentations or complications thereof might have been a factor in rupture because one patient had a transverse position and the other had the baby presenting by the vertex, but there was edema of the meninges present. It is interesting to note that in the two patients who went into labor, cervical dilatation was poor because of weak pains.

TABLE VII. PROBABLE CAUSE OF UTERINE RUPTURES

I. Intrinsic:	
A. Changes in uterine muscle cells	2
B. Fibrosis postcesarean section	3
C. Congenital abnormalities	1
II. Extrinsic:	
Associated with manual or instrumental manipulation during the labor	6

TABLE VIII. RUPTURE IN NONCESAREAN SECTION CASES (9)

Type:	
Complete	6
Incomplete	3
Site:	
Left side	5
Right side	2
Anterior wall	0
Summit of fundus	1
Unknown	1
Cervix:	
Involved	5
Not involved	2
Not stated	2
Time from delivery to diagnosis:	
Immediate	4
Delayed	2
Not stated	3
When rupture occurred	All during second stage

Patients not previously subjected to cesarean section had complete ruptures twice as often as incomplete ruptures.

## MORTALITY—FETAL AND MATERNAL

*A. Fetal.*—Of the twelve cases, there are ten to consider because in one there was a five weeks' embryo and in another, the status of the fetus is not given. Three living children were obtained and seven stillborn. However, in previous cesarean section cases, all three children died, a mortality of 100 per cent; in noncesarean section cases, the mortality was four in seven. Reports in the literature vary: Lobenstine<sup>6</sup> 70 per cent; Michailoff<sup>2</sup> 93 per cent; Davis<sup>3</sup> finds an 80 per cent fetal mortality in previous cesarean section cases and those without a previous cesarean section alike; McNeile and McBurney<sup>8</sup> find 60 per cent in cesarean section cases and 65 per cent in noncesarean section cases.

*B. Maternal.*—One death, in twelve cases, or a mortality of 8.5 per cent, occurred. It is worthy to note that this case was an incomplete rupture of the uterus which was not operated upon but treated by intrauterine packing. Sandler<sup>9</sup> quotes Weber as finding 70.8 per cent mortality in 1910 and Kupferberg 66 per cent in 1927; Davis<sup>3</sup> has a general mortality of 60 deaths in 106 cases or 56.6 per cent, but previous cesarean section cases alone have a mortality of only 12.5 per cent; Sachs<sup>2</sup> 60 per cent; Snequireff<sup>2</sup> 48 per cent; Sakharoff<sup>2</sup> 50 per cent; McNeile and McBurney<sup>8</sup> 20 per cent mortality in previous cesarean section cases and 90 per cent in cases not subjected to previous cesarean section.

## SYMPTOMS AND DIAGNOSIS

These cases show that rupture of the uterus can occur without dramatic phenomena commonly described. In 3 cases, the severity of the symptoms were not described in detail; therefore, only 9 are to be considered. Of these, 5 had no symptoms whatsoever and diagnosis was made by vaginal examination following the operative delivery in 4 and when cesarean section was being performed on the other, a previously sectioned case. Four patients had symptoms; 2 were operative deliveries showing postpartum signs of shock, pain in the left chest, weak pulse; 2 previously sectioned patients had no signs of shock but demonstrated only increased pulse rate, growing weaker, and pain in the abdomen. Thus, shock is to be expected in only 33.3 per cent of rupture cases and not at all in patients having a previous cesarean section.

## SUMMARY

The causes of uterine rupture fall into two groups:

- a. *Extrinsic overdilatation type*: which is accompanied by some obstetric maneuver such as version and extraction, craniotomy, or forceps.
- b. *Intrinsic type*: which includes congenital abnormalities of the uterus, fibrosis, postsection and various changes in uterine muscle cells from numerous causes.

Conservative obstetrics and repeated section if labor does not terminate quickly and successfully will prevent most ruptures of the uterus. This prophylaxis is the best form of treatment. Hysterectomy is the operation of choice for uterine rupture above the cervix; previous cesarean section cases that tear should be re-sutured and sterilized if necessary.

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## A HISTOPATHOLOGIC STUDY OF A CASE OF INTRA-FOLLICULAR OVARIAN PREGNANCY\*

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THE occurrence of a case of primary ovarian pregnancy is sufficiently rare to warrant recording, although the number of case reports in the literature is steadily increasing.

Mrs. E. A., colored housewife, twenty-four years of age, was admitted to the hospital, March 16, 1916. Her chief complaint was "excessive menstruation."

She was married five years, husband living and well. She has two children in good health, three years and sixteen months of age, respectively. Her last confinement was Oct. 24, 1915, and was normal. She nursed her last child up until the time she entered the hospital. No miscarriages.

*Menstrual History.*—Menstruation began at fourteen years of age, occurred every twenty-eight days, and the flow lasted from five to seven days. Menstruation was always painful on the first day.

*Present Illness.*—Patient states that on Feb. 18, 1916, she had cramplike pains and began to flow. About two days later she passed a "fleshlike" mass, and the flow was rather excessive. This continued for a period of two weeks, during which time she passed many large clots. She took some medicine from her family physician and the flow stopped for five days, after which time it started again, although the clots were smaller, and she then decided to enter the hospital. At the time of her admission the flow was painless, but she felt very weak.

*Physical Examination.*—On March 15, the day of her admission, showed a small woman with pale mucous membranes, who was obviously very weak. Temperature 98.6°, pulse 90, and respirations 20. Heart and lungs were normal. Blood pressure 110/80. Red blood cell count was 3,400,000. Hemoglobin 65 per cent (Sahli). White cell count 8,200. On bimanual examination, a freely movable, painless mass was felt in the region of the left ovary. It was about the size of a lemon. The diagnosis of left ovarian cyst was made.

*Operation.*—Laparotomy operation was performed on March 28, 1916, by Dr. W. A. Warfield, and what seemed to be an ovarian cyst and part of the fallopian tube was removed. Upon section of the mass after operation, a fetus within a sac in the ovary was found. Her operative convalescence was uneventful.

*Macroscopic Pathologic Examination.*—The specimen consisted of an enlarged left ovary, fallopian tube, and mesosalpinx.

*Left fallopian tube* was 6.7 cm. in length. It measured through the ampulla 7.5 mm., which was its greatest diameter, while through the sectioned uterine end it measured 4 mm., which was its smallest diameter. All the fimbriae were free and appeared normal. The fimbria ovarica was well defined, free from adhesions, and connected the fimbriated extremity of the tube to the ovary. The ostium abdominale was patent. The tube was of a yellowish gray color, excepting at a point about 2.5 cm. from its uterine end, over which area the tube was dark red in color (due

\*For lack of space it is not possible to include all of the authors' confirmatory illustrations.

to clamping at the time of operation). The tube was tortuous but apparently normal, except for the dark red area mentioned above. There were no adhesions, kinks, or any evidence of rupture.

*Mesosalpinx* contained in its outer part a rather well marked oöphoron, and appeared normal.

*Left ovary* was a somewhat irregular oval mass measuring 6 by 4.5 by 3.6 cm. Several low roundish elevations, varying in diameter from 1.5 to 3 cm., form part of its outer surface, while the remainder of this surface presented numerous smaller roundish elevations, that varied from 2 mm. to 1 cm. in diameter. Some of these smaller dome-shaped swellings occurred upon the tops and sides of the larger elevations. These smaller elevations were cystic, and most of them were yellow in color, although a few were the color of chocolate. The yellowish colored ones yielded when opened a thin yellowish fluid, while the dark colored ones contained a coagulum of old blood. A smooth and somewhat glistening membrane covered the surface of these cysts as well as the intervening depressions. This membrane (*tunica albuginea*) presented no adhesions, but beneath it several small and very tortuous blood vessels coursed for short distances at different places. One relatively large vessel was seen which became evident about the middle of the inferior aspect of the ovary and ascended vertically on the posterior surface, then divided into three smaller branches, each of which after a very tortuous course disappeared within the ovary at or near the base of one of the cystic swellings. The ovarian ligament was about 5 mm. in length from its sectioned end to its ovarian attachment. It appeared normal.

On vertical section there was seen, situated near the center of the ovary, an oval cavity which measured 2.1 by 2.2 cm. in its vertical and transverse diameters, respectively. Its greatest anteroposterior diameter was 1.9 cm. The cavity contained a small embryo and was filled with liquor amnii. The embryo was attached to the cavity wall by a short cord. The cavity was lined with a glistening amniotic membrane. The tissue surrounding this cavity was reddish brown in color, and fairly firm in consistency. Near the external surface of the ovarian mass were a few small cavities, resulting from incisions of some of the small cysts, seen on the external surface of the mass. The cavity was located at a distance of 6 mm. from the inferior surface of the ovary: that is, the thinnest portion of the sac wall, at which point was the attachment of the placental anlage (where the cord joined with the amnion). A distance of 1.9 cm. separated the cavity from the superior surface of the mass: this represented the greatest distance of the cavity from the external surface, or the thickest portion of the sac wall.

The embryo measured, from the extreme tip of its cephalic end to the tip of its caudal end, 15.5 mm.; this was with its body bent. It measured from the small projection, which occurred just below the head to its caudal extremity, 12.5 mm. Its body was somewhat flattened transversely, which increased the anteroposterior diameter, and diminished the transverse diameter. The anteroposterior diameter, just above the umbilical region, was 7 mm., while the transverse diameter was 4 mm. throughout. Four small limb buds, indicating the site of future extremities, were present. The optic vesicles were seen as two very dark circular spots on each side of its head. Its sex could not be differentiated. A part of the amnion covered the upper part of the body of the embryo. The cord presented one twist; it measured 7.5 mm. in length and 15.0 mm. in diameter. When the specimen was immersed in water, the cord kept the embryo, which floated, attached to the sac wall. There was no macroscopic evidence of a placenta. The cord joined with and apparently became continuous with the glistening amniotic membrane lining the wall of the cavity.



*Microscopic Pathologic Examination.*—The specimen was preserved in Craig's solution. The pieces of tissue removed for microscopic study were washed in running water for two days, so as to rid them of all traces of Craig's solution. They were embedded in paraffin, stained with hematoxylin and eosin, and mounted in Canada balsam. Sections were made through the uterine end of the tube, the middle of the tube, just inside of the fimbriated extremity of the tube, and through



Fig. 1.—Oil immersion view of a villus in direct contact with ovarian tissue

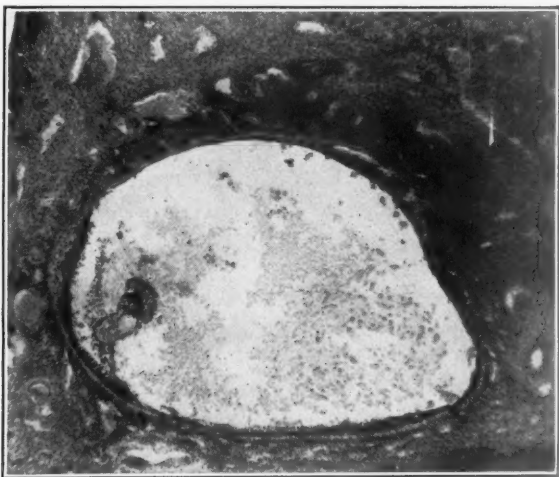


Fig. 2.—Low power. Ovarian stroma with graafian follicle, which contains a partial cumulus oophorus. This section is from the thickest part of the sac wall.

the fimbriated extremity. One section was taken from the mesosalpinx subjacent to the fimbriated extremity. Sections were taken from 10 different places in the sac wall, each equidistant from the other. One section was taken from the sac wall at the point where the cord became continuous with the amnion, i.e., site of placentation.

*Left fallopian tube:* The mucosa in all sections was normal. The muscular layers were well defined and normal. There were no decidual cells, nor was there any

evidence of inflammation. Outside the muscular layer in two sections, there was some extravasation of blood between the two layers of the broad ligament (due to trauma at operation). The fimbriae were normal.

*Mesosalpinx* was represented by a number of blood vessels and a few epithelial-lined tubules surrounded by connective tissue. Many of the arteries were well developed, as shown by their marked muscular walls. No inflammatory reaction or hemorrhage was noted.

*Sections from the sac wall* showed internally fetal membranes, externally ovarian stroma, separated by a blood clot which comprised the greater part of each section.

*The fetal membranes* were composed of a normal amnion that was intact, in which the clear cuboidal epithelial cells were characteristic. The amniotic mesenchymal layer blended in many places with the chorionic mesenchymal layer; elsewhere it was connected by a few delicate strands of connective tissue. The cells constituting the amniotic and chorionic connective tissue were for the most part spindle-shaped, although in places some were stellate. Adjoining the chorionic mesenchymal layer was a well-marked trophoblast; the cells comprising it had round small or oval nuclei rich in chromatin. The cytoplasm was clear. These cells occurred in groups, a few singly, separated by blood spaces. A small amount of canalized fibrin was present associated with these cells. The cells were polygonal and sent out rayed processes.

*The layer of blood clot:* This layer made up most of the wall of the gestation sac; beginning with the trophoblast internally, it extended to the limiting ovarian stroma externally. Concentric lamellation was present. Each section showed numerous chorionic villi, completely surrounded by red blood cells in the intervillous spaces. Many villi were normal; others showed degenerative changes. The external syncytial layer with an internal layer of cuboidal Langerhans cells was distinctly seen in many of the villi; some showed only the Langerhans cell layer, while in others only the syncytium could be made out. Myxomatous tissue completely filled some of the villi; other villi showed one or more thin-walled small blood vessels containing erythrocytes. The Langerhans cells were clumped in places, forming several rows of nuclei. The syncytium sent out pointed processes here and there into the blood clot. In a few places villi were seen beginning as out-shoots from the trophoblast. In one section one or two villi were seen in direct contact with the ovarian stroma, without any interposition of blood or fibrin. The degenerating villi did not take the stain well, and the cell outline was lost. The nuclei were entirely absent in many places, while in others the nuclear chromatin was represented by numerous small granules scattered throughout the cytoplasm, which stained deeply with hematoxylin. Hyaline degeneration was present in some. Some of these necrotic villi were completely surrounded by polymorphonuclear leucocytes, which also had replaced the myxomatous core of these villi. All stages of cell destruction to absolute cell disintegration and disappearance were present. A well-defined fibrin layer was present in the outer zone of the blood clot, which lay between the villi and the ovarian stroma except in one section where the villi were lying in the ovarian stroma.

*Foci of necrosis and leucocytic infiltration* interrupted the continuity of the fibrin layer in a few places.

*Ovarian stroma:* This formed the external boundary of the blood clot. It was thickest near the hilum and became very thin below. It was thinnest opposite the point where the cord became continuous with the amnion, at which site it was represented by a layer of cells about a dozen rows in thickness. These cells were flattened out as a result of pressure exerted by the clot and contained very few blood vessels. The stroma was intact throughout, and showed no point of rupture. The stroma near the hilus was most abundant and showed little or no pressure changes. Here it was very vascular; many of the blood vessels contained red blood cells;

some were empty. The muscular coats of the arteries were very thin in places and showed many hyaline changes in the media. Small areas of extravasated red blood cells were present here and there in the ovarian stroma. Two sections from the cortex from different portions of the sac wall exhibited graafian follicles. Three were present in one section, and appeared normal. One of the follicles was 3 mm. in diameter. Two follicles showed the membrana granulosa with an external and internal tunica, and portions of a cumulus oophorus. One follicle showed an undeveloped ovum. In another section a relatively large follicle was flattened out by pressure and in it one could make out only the membrana granulosa and the tunica internus and externus. Several primordial follicles were seen in this section. Two sections from different portions of the sac wall showed corpora albicantia—one was of relatively large size; these sections contained no follicles. In the section that showed villi within the ovarian stroma, there were noted groups of polygonal cuboidal cells with round, central, deeply staining nuclei, that had a pale cytoplasm. It was easily apparent that they were not stroma cells, and on close scrutiny it was seen that they were derived from the Langerhans cells of the villi; and in places the connection between these cells and the villi could be made out. In the stroma areas nearest the blood clot and especially near the hilus were groups of altered lutein cells; they had lost their yellow pigment. The cells were relatively large, polyhedral or octohedral in shape, with a cytoplasm that did not stain. The nucleus was central, and contained a definite nucleolus. In other portions of the stroma, which showed the greatest pressure changes, these cells occurred often in single rows surrounded by stroma, and their characteristic morphology was not so evident. At the edge of the blood clot, they frequently occurred singly surrounded by hyalinized connective tissue. Many showed degenerative changes; vacuolation was the most frequent alteration. A few of the cells showed yellow pigment, which, however, was not the characteristic pigment of lutein cells. The preserving fluid probably dissolved out the pigment from these cells. Hyaline degenerative changes of the stroma was present in many places. In certain places there was marked proliferation of the stroma connective tissue along the edges of the blood clot; the young fibroblasts extended into the clot in many places, representing an attempt and organization. Foci of necrosis and leucocytic infiltration were also scattered throughout the stroma; the leucocytes undoubtedly acting as phagocytes. In one section numerous eosinophiles were present in the stroma. The layer of germinal epithelium on the external surface was represented by groups of cuboidal cells here and there on the free surface of the ovarian cortex, among which no germ cells were distinguishable. There was no evidence of a tunica internus or externus surrounding the gestation sac. The site of placentation showed only villi and intervillous spaces filled with blood. There were no decidual cells seen in any of the sections. There was nothing in this case to suggest endometriosis as a causative factor.

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**Ch'en, K. C.: A Case of Pregnancy at Term Complicated by Complete Atresia of the Vagina, Chinese M. J. 50: 917, 1936.**

The patient in the third month of pregnancy went to a woman in her native town, who gave her a medicated tampon for vaginal application in the hope of inducing an abortion. The tampon contained some caustic material, probably a crude potash preparation. The application resulted in complete atresia of the vagina necessitating a cesarean section, followed by total hysterectomy. Recovery was uneventful.

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## AUTOTRANSFUSION WITH BLOOD FROM LARGE MYOMATOUS UTERI

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TRANSFUSIONS are often employed for the satisfactory recovery of patients who have had myomatous uteri removed. In this paper I am presenting a practical method for autotransfusion in which the blood in the myomatous uteri is recovered and returned to the patient. This procedure, used successfully in two cases, has been prompted by the following observations: first, a large amount of blood almost invariably escapes from the specimen after it has been removed and placed in a basin, and second, the presence of frequently engorged subserosal veins of uteri containing large myomas.

The advantages of this method are that there is no necessity of another donor and the blood is immediately available when urgently needed.

Cottis,<sup>1</sup> in his discussion of the value of auto blood transfusion, states: "In the event of severe hemorrhage into the abdominal cavity, whether it is before or during operation, it is not good surgery to throw away the blood. This method of returning it to the patient is simple, safe, and effective. It is a conservative measure which is worthy of more general use."

Moreover there is no fear of the foreign protein reaction which may follow in so-called true blood matching.

Levine and Segall<sup>2</sup> in their studies on posttransfusion reactions state: "A long operation in which ether is used alters the patients' serum as regards its hemoagglutinin properties. This is not permanent but disappears in the first twenty-four hours after operation."

Autotransfusion, autohemofusion, and autoinfusion are used synonymously in the literature. Autotransfusion was employed successfully in 1914 by Johannes Thies<sup>3</sup> of Leipzig. He reported three cases of ruptured ectopic pregnancy where he procured the blood free in the peritoneal cavity and returned it intravenously to the patient. Previous to this time the English mentioned the advisability of autotransfusion and used it in several cases of leg amputations. Lichtenstein<sup>4</sup> in 1918 reported its use in 39 cases of extrauterine pregnancy. The first article on this subject to appear in this country was published by White<sup>5</sup> in 1923. Autotransfusions in ruptured tubal pregnancies have been reported by May,<sup>6</sup> Cottis,<sup>1</sup> Maynard and Rees,<sup>7</sup> Appleby,<sup>8</sup> Love,<sup>9</sup> and Ricci and Di Palma,<sup>10</sup> and others. In 1923 Burch<sup>11</sup> summarized 164 cases, all European, with only two deaths. Davis and Cushing<sup>12</sup> described a method for autotransfusion, using the blood lost during prolonged neurosurgical operations. Gray<sup>13</sup> obtained the blood after splenectomy and used it with good results. Coley<sup>14</sup> reported a case of autotransfusion where the blood from a traumatic ruptured spleen was employed. Recently Watson and Watson<sup>15</sup> reported the successful use of autotransfusion in the treatment of a patient who had a laceration of the heart.

Blood for autotransfusion has been obtained by various methods, treated in many different ways and administered to the recipients by a variety of technics. In gynecology and general surgery, the blood escaping from tubal pregnancies or from ruptured viscera has been allowed to remain in the peritoneal cavity for absorption. At other times it has been removed from the peritoneal cavity by a suction apparatus or a syringe or has even been dipped up by cups or squeezed out of tampons and then returned to the patients' veins. In general medicine, especially in blood disorders, it has been procured from the patients' veins, treated by radium, x-ray, chemicals, or kept in an incubator before being returned to the circulation. In obstetrics, blood obtained from the placenta has been given by rectum. Farrar<sup>16</sup> in her article, describes a technic similar to the one employed by me. She used this form of transfusion in patients where blood had escaped into the peritoneal cavity during hysterectomy and from tubal gestation.

Sampson<sup>17</sup> in two articles published several years ago showed, by the injection of the blood vessels of myomatous uteri, that there is a great increase in the blood supply of uteri containing these tumors and that the subserosal veins of the uterus and tumors are greatly enlarged. MacFee<sup>18</sup> states: "It is a matter of common observation that fibromyomata of the uterus, whether pedunculated or sessile, frequently present large, tortuous, thin walled, subserous veins. It occasionally happens that one of these large vessels becomes ruptured producing serious intraperitoneal hemorrhage." These engorged veins are readily accessible for recovering the blood present in the large myomatous uteri.

In order to learn how much blood may be removed with uteri which contain myomas and also with uteri which are free of gross pathologic changes, the following data were collected by me and are presented in the accompanying tabulations. During panhysterectomy the blood supply of the organ was cut between clamps or sutures so that whatever blood the organ contained was removed with it. As soon as the specimen was removed, it was placed in a basin, the clamps or sutures were removed and the blood was allowed to escape from the uterus. Forty uteri were studied in this manner. Twenty-five of these uteri were grossly normal and had been removed for various reasons. The remaining fifteen uteri contained myomas of various sizes. The normal-appearing

TABLE I. THE WEIGHT AND AMOUNT OF BLOOD IN MYOMATOUS UTERI

HOSP. NO.	AGE OF PATIENT	WT. OF UTERUS IN GM.	AMOUNT OF BLOOD DRAINED C.C.
6881	47	2830	270
12380	48	4100	425
6788	46	2100	20
453	44	2730	220
1185	28	840	24
25442	45	2690	240
422-35	55	1810	250
4749	47	3960	410
10840	38	2230	210
2786	46	1360	100
1907-35	42	1580	200
5403	47	1360	160
10140	36	1910	270
276-35	42	2880	380
8599-33	46	9971	950



uteri weighed from 95 gm. to 152 gm. and yielded not more than 5 c.c. of blood. The fifteen uteri containing myomas weighed from 840 gm. to 9,971 gm. and drained from 20 c.c. to 950 c.c. of blood.

Obviously there is a fairly constant amount of blood drained from a normal-sized uterus, while the blood obtained from myomatous uteri using similar methods is greater. Moreover, the amount of blood obtained from a myomatous uterus is not directly proportional to the size of the tumor. Even fairly large myomatous uteri may sometimes contain very little blood, as shown in Table I.

#### TECHNIC

In the two cases reported in this paper blood was obtained from myomatous uteri before removal but after their blood supplies had been ligated or clamped and

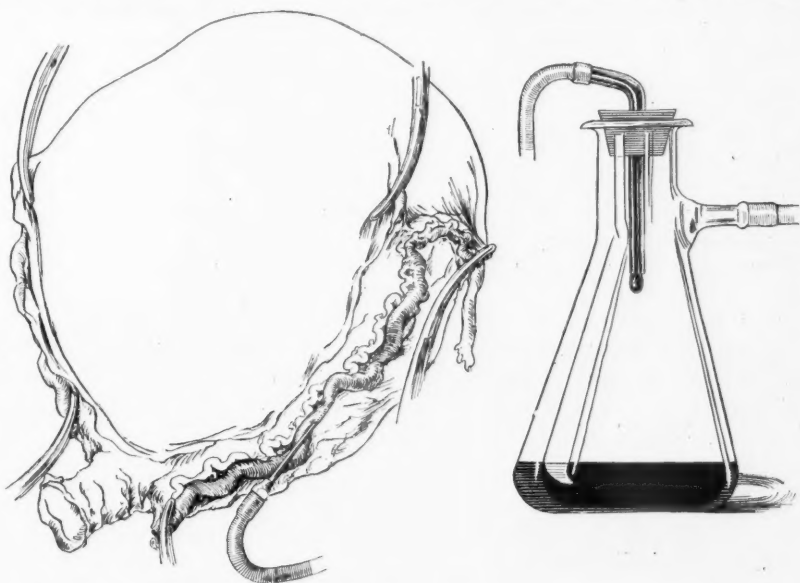


Fig. 1.—A large myomatous uterus after its removal is shown. A needle is inserted in a large uterine vein between the layers of the broad ligament. The flask at the right is situated on the instrument table. The tube inserted in the rubber stopper of the flask is a continuation of the tube with the needle inserted in the vein. The tube from the side limb of the flask is continuous with the bottle on the floor near the radiator. Another tube extends from this same bottle to the radiator which is the source of suction.

then immediately returned to the patients' circulation by intravenous transfusion. The apparatus used for recovering the blood from these myomatous uteri is a suction outfit similar to the one ordinarily employed in recovering fluids in the course of abdominal operations. This consists of a source of suction which, in the operating room of the Albany Hospital, is the radiator. A large bottle with a two-holed rubber stopper is placed on the floor near the radiator. Through one opening in the stopper a glass tube with a rubber delivery tube is attached to the source of suction. Through the other opening a tube is connected with a suction flask on the instrument table as shown in Fig. 1. The suction flask on the instrument table is plugged with a one-holed rubber cork. From a side limb in the flask a tube is attached to the source of suction. Through the hole in the rubber stopper a tube with needle at-

tached is extended to the specimen. The suction flask and tubes are all sterilized before operation. The instrument nurse washes out the flask and tubing with normal saline and then places 40 c.c. of 2 per cent sodium citrate solution in the flask. It is now ready for use. In the cases reported, a No. 12 gauge needle was inserted in the large subserosal veins of the uterus and those of the mesosalpinx. These veins were very large in both cases. Continuous suction could not be employed because the wall of the vein would collapse against the opening in the needle. This difficulty was overcome by compressing the tube and shutting off the suction and allowing the veins to be filled by gravity or massage. In the first case 500 c.c. of blood was obtained from the uterus and in the second case 380 c.c. of blood.

The operator can proceed without difficulty while the suction is working. Now and then the instrument nurse rotates the flask containing the blood, citrate, and saline solutions. After sufficient or all the blood is obtained, the instrument nurse filters the blood through at least twenty thicknesses of gauze and measures it. If more of the 2 per cent citrate is needed to make the citrate solution 10 per cent of the total volume, the necessary amount is added. While the blood is being prepared, an interne starts an intravenous injection of normal saline, so that he is ready to give the citrated blood as soon as it is filtered. The blood is kept at body temperature by immersing the flask in warm water. In the two cases reported by me, the transfusion was completed before the abdominal operation was finished. On account of the possibility of malignancy being present in a myomatous uterus, either in the form of sarcoma or an associated adenocarcinoma of the uterine mucosa, even in women before the menopause, it would be wiser to collect the blood, but not use it until after the uterus has been removed and incised. If necessary, frozen sections can be made and examined.

Although the cubital vein has usually been used, any vein, even a large vein of the omentum, can be used if the brachial vessels are collapsed and the abdominal cavity is exposed.

Citrated blood has been used without danger. When one considers that if 1,000 c.c. of citrated blood are given, the patient receives only 2 gm. of sodium citrate. This method may be considered feasible since over twice that amount of sodium citrate may be safely given to the patient.

#### CONTRAINDICATION TO THE USE OF AUTOTRANSFUSION IN GYNECOLOGIC OPERATIONS

The contraindications to autotransfusion are three: infection, malignancy.

A careful examination of the peritoneal cavity for evidence of infection should be made at the time of operation. If any such evidence is found, the blood should not be used. It is also possible that bacteria may be introduced into the blood stream of the patient as a result of faulty technic.

The greatest contraindication to this procedure in myomatous uteri is the possible presence of sarcomatous changes in the myoma or an associated carcinoma of the uterine mucosa. A large percentage of women between thirty and forty years of age have uterine myomas. Some of these will have malignant changes of the uterus in later years. Since uncomplicated myomas usually decrease in size after the menopause, any increase in size of a myomatous uterus after that time should be looked upon as an indication of possible sarcomatous change in the myoma.

Approximately 80 per cent of the patients with cancer of the body of the uterus are past the menopause. This coincides with the percentages obtained from my study<sup>19</sup> of the cases of carcinoma of the body of the uterus occurring in the Gynecological Service of the Albany Hospital from 1921 to 1931. A large percentage of the patients with cancer of the body of the uterus also have uterine myomas. In view of the above clinical data, any woman at or after the menopause who complains of uterine bleeding, even if myomas are present, should have either a panhysterectomy or a diagnostic curettage if for any reason the former is contraindicated. In the latter instance, the blood of the specimen should not be used for transfusion purposes if malignant changes are present in either the endometrium or myometrium. If there is any suspicion of the possibility of either form of malignancy being present in a case the blood may be obtained and kept until a microscopic report of a frozen section is secured.

#### REPORT OF CASES

CASE 1.—Mrs. R. J., aged forty-six years (No. 8599-33), married and the mother of three children, was admitted to the Albany Hospital, Nov. 25, 1933, complaining of incontinence of urine while standing, enlargement of the abdomen, weakness, and prolonged profuse menses. Her present history dates back at least six years when she was seen by a physician who told her that the enlargement was due to a pregnancy. Menstruation began at the age of fourteen years and has always been regular, the flow lasting from four to five days. During the past year the flow has increased in amount and duration and recently has given rise to the symptoms of secondary anemia.

The patient was well nourished but her mucous membranes were pale. She had dyspnea on slight exertion, even talking. The heart and lungs were normal. The abdomen was enlarged by a tumor mass arising in the pelvis and extending to the ensiform cartilage. This mass was hard and the percussion note over it was dull. There was tympany in the flanks. There was slight edema of the extremities. Pelvic examination showed that the tumor was evidently of uterine origin. The examination of the urine was negative. The blood Wassermann test was also negative. Her hemoglobin was 50 per cent, white cell count 10,000, and red blood cells 3,950,000.

The patient was given the usual preparation for operation and matched for transfusion. Three acceptable donors were made available. Under ether anesthesia, a large myomatous uterus was found extending to the diaphragm and not adherent, with subserosal veins 1 cm. in diameter. The entire uterus, both tubes and ovaries, and the appendix were removed by Dr. J. A. Sampson.

During the operation, after the blood supply of the uterus had been clamped or ligated, 500 c.c. of blood were obtained by me from the uterus by first inserting a No. 12 gauge needle into available large veins, including the large subserosal, the uterine veins, and the veins of the mesosalpinx, and then aspirating the blood by suction. Since the blood would not fill the veins as readily as if the arterial supply were intact, it was obtained by alternately applying suction and allowing the veins to fill by external pressure. The blood was citrated, filtered and given intravenously to the patient by gravity. After the removal of the uterus and cervix, 450 c.c. of blood were obtained by allowing it to drain from the tumor. This blood was not

used because of the fear of contamination from the cervix. The uterus, after the removal of the blood, weighed 9,971 gm. The patient was discharged in good condition on Dec. 23, 1933.

CASE 2.—Mrs. H. K., aged forty-two years (No. 276-35), and the mother of one child, was admitted to the Albany Hospital, Jan. 8, 1935, complaining of profuse, vaginal bleeding of four weeks' duration, increasing weakness, and shortness of breath. Her menstrual periods began at the age of fourteen, recurred at intervals of twenty-eight days and lasted for about five days. However, in the past few months, the flow had been increasing in amount and duration. The only other significant fact in her history was a loss of twenty pounds in the past six months. This, she explained, was due to a self-regulated rigid diet.

The patient was well developed and well nourished. Her heart and lungs were normal. The abdomen was moderately distended by a hard, firm tumor mass which extended from the symphysis to about two fingerbreadths above the umbilicus. Hemoglobin was 54 per cent and red blood count 3,400,000.

Under ether anesthesia, a large multinodular myomatous uterus and the left tube and ovary and appendix were removed by Dr. Sampson. After its blood supply was ligated, 380 c.c. of blood were obtained from the uterus. This blood was properly citrated, filtered and returned to the patient's circulation. The patient made a normal convalescence and was discharged Jan. 27, 1935, in good condition. The uterus, after the removal of the blood, weighed 2,690 gm.

#### SUMMARY

1. Autotransfusion is a standard procedure in the Gynecological Service of the Albany Hospital.
2. In selected cases blood may be obtained from a myomatous uterus during the operation or after the uterus is removed and returned to the patient intravenously as soon as the operator is sure that malignancy is not present in the uterus.
3. A simple technic for this purpose is described.

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## UTERINE PAPILLARY CYSTADENOMA OF WOLFFIAN BODY ORIGIN

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A SURVEY of the literature of the last twenty-five years reveals a prodigious number of articles under the headings of "adenomyoma" and "adenomyosis" of the uterus, but few cases, if any, of true papillary cystadenoma of the uterus have been described as such.

C. J., Porto Rican, thirty-eight years of age, married for fourteen years, was admitted to the Cumberland Hospital of Brooklyn on March, 1935, complaining of a mass in the lower abdomen for two years. She had no pain or other associated symptoms and was normal in every respect. Menstruation began at the age of fourteen. She was menstruating at the time of admission to the hospital and her last normal

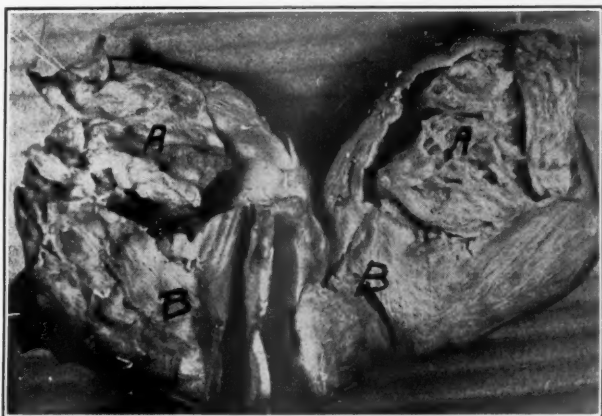


Fig. 1.—Gross specimen showing tumor (A) situated in the upper portion of the uterus (B).

period occurred a month previously. She had one pregnancy which ended in a spontaneous miscarriage (date unknown). Abdominal examination revealed a movable mass, about 9 by 12 cm., in the lower abdomen, arising from the pelvis, which by bimanual examination was apparently part of the uterus. No tenderness was noted in either the region of the mass or the uterus. The cervix was in the vaginal axis and the adnexa were not felt.

The blood Wassermann and the Aschheim-Zondek tests were negative. *Preoperative diagnosis:* Fibromyoma uteri. *Operative diagnosis:* Fibromyoma uteri and chronic bilateral tuboovarian disease. *Operation:* Supracervical hysterectomy, bilateral salpingo-oophorectomy. The wound healed by primary union and the patient made an uneventful recovery.

### PATHOLOGIC REPORT

*Gross specimen:* (Fig. 1.) Consisted of uterus and adnexa. The uterine wall was smooth and ovoid in shape, soft in consistency, and the uterus measured 10.5 cm. in length, 7.5 cm. in width, and 5.5 cm. in anteroposterior diameter. The





Fig. 2.—Section through the tumor proper, showing the papillary cystadenomatous character of the growth.



Fig. 3.—Section through the interstitial portion of the right tube. Note wolffian tubules (*A*) along the course of the fallopian tube, part of the lumen of which (*B*) appears in the section.

specimen was opened from the right lateral surface. The endometrial cavity was found to be a narrow, crescentic slit which extended to a height of 3 cm. from the lower pole. The cavity could be traced to the left tube, but on the right side it was lost and its continuity could not be established with the right tube.

An intramural, pale pink, cystic, trabeculated mass 5 by 6 by 4 cm. occupied the greater portion of the uterine body and fundus, and contained a large number of discrete cystic structures of varying size which were mucoid in appearance and were filled with a clear colorless fluid. The main wall was completely surrounded by myometrium and merged imperceptibly with it.

The tubes were thickened, cystic, and retort-shaped. The fimbriated ends were sealed. On section, the tubal lumina were found to contain a viscid, chocolate-colored content.

The ovaries were small, intimately adherent to the tubes, and on section presented a sclerotic appearance, with several small follicular cysts, and hyalinized corpora albicantes.

*Microscopic:* (Figs. 2 and 3.) The tumor was composed of interlacing cystic and papillary structures which were lined by epithelium, varying from low cuboidal to tall columnar, both ciliated and nonciliated cells, and supported by a stroma of muscle and connective tissue, but nowhere in the stroma could endometrium be demonstrated. Serial sections failed to establish continuity between the newgrowth and the endometrium. Sections through the interstitial portion of the right tube and including a small area of the cystic mass disclosed the interstitial portion of the tube, and there were in its vicinity numerous ducts and glandlike structures, varying in size and shape. They were lined by cells which were both ciliated and nonciliated and which varied from low cuboidal to tall columnar, directly imbedded in the muscle tissue of the uterus, with no communication with the tubal lumen. These structures were histologically recognized as epoophoron-like (wolfian body rests). A number of these ducts and glandlike structures were cystic, some were papillated and showed a striking similarity to the histologic picture of the uterine intramural newgrowth described above. The tubal walls presented a chronic inflammatory process. Sections of the ovary showed a chronic oophoritis and several follicular cysts.

#### DISCUSSION AND CONCLUSION

In the opinion of the authors, this tumor is probably of wolfian body origin. Notwithstanding Cullen's view that one cannot differentiate from the histologic picture a wolfian or müllerian origin of intramural cysts, the histologic picture of this newgrowth is apparently not of endometrial or tubal origin as evidenced by (a) the failure to trace continuity to either of these structures by serial sections as well as by (b) the absence of endometrial stroma in the tumor. On the contrary, the histologic picture of the newgrowth more closely simulates that of the epoophoron (wolfian body rests). This is in conformity with the observation of Ivanov, whose work shows the part played by the wolfian body in the formation of the uterine wall. Mercadé has demonstrated that the location of these wolfian body rests may be at the cornua, in the fundus, or along the lateral wall of the uterus. The structure and location of the mass in this case therefore may be considered a papillary cystadenoma of wolfian body origin and as such should be recognized as distinct from the adenomyomas of heterologous origin.

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## DIABETES INSIPIDUS AND PREGNANCY

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**D**IABETES INSIPIDUS has been studied extensively, but infrequent mention is made of pregnancy as a complicating factor. It is not the purpose of this case report to analyze the literature in great detail. Momigliano<sup>1</sup> (1929) in an extensive monograph, collected a total of thirty-one cases from the literature to that date and reported two cases of his own. Since then, three further cases (Anselmino and Hoffman,<sup>2</sup> Artaud,<sup>3</sup> Dietel<sup>4</sup>) have been reported. Findings of significance have been: (a) Consistent lack of relationship to possible pituitary lesions as demonstrated by x-ray changes in the sella turcica, (b) infrequent relationship to positive Wassermann, (c) rather frequent incidence of premature labor, and (d) uniform response to posterior lobe pituitary medication. The possible undesirable effect of extensive use of posterior lobe extracts during pregnancy, especially during the latter months of gestation, must be considered.

Diabetes insipidus may be present before the onset of pregnancy or the disease may make its appearance during gestation. In the latter state (diabetes insipidus gravidarum) subsequent to the termination of the pregnancy the diabetes insipidus may disappear or remain as a disease condition. The number of cases of diabetes insipidus present only during pregnancy and absent during the interim between pregnancies is rare. Thus the pregnancy is usually considered as purely coincidental. The case reported here was one in which conception took place about three months after onset of the diabetes.

G. van I., white, thirty years old, no constitutional disease, in good health. Measles was the only childhood disease. Patient married fourteen years. Seven previous pregnancies, three of which were observed in this clinic, all uneventful. Menstrual history normal, last regular period, Dec. 6, 1933. Flowed scantily in January, February, and March, 1934. This oligomenorrhea was an associated finding and was not due to pregnancy.

Weight averaged 152 pounds, present 182 pounds, entire gain since onset of present illness.

In the latter part of December, 1933, the patient noted a sudden thirst. From that acute onset, when she felt otherwise well, continued a severe polydipsia and polyuria. The intake and corresponding output was 12 to 14 quarts of fluid per day. The Jan. 9, 1934, menstrual period was very scant, an unusual occurrence with her, so she came to the Washington University Clinics for the first time on Feb. 16, 1934. It was thought that she was not pregnant. She was referred to the Medical Clinic because of the polydipsia and polyuria. An intranasal application of pituitary extract (posterior lobe) was administered with prompt relief for three hours. The patient was transferred to Barnes Hospital for observation and study.

Physical examination showed a well-developed, obese, white woman; short, broad physique, weight 182 pounds. Normal in all respects except as noted. Basal metabolism rate, 6 per cent, plus. Blood Wassermann, Kahn, Kline, negative. Average fluid intake before onset of medications was 7,000 to 14,000 c.c. a day with an average urinary output of 10,500 c.c. The specific gravity of the urine was 1.0005 to 1.005.

TABLE I. BLOOD CHEMISTRY

DATE	UNDER Rx	HB %	C.V. %	B.S. MG. %	N.P.N. MG. %	CL. MG. %	PROT. MG. %	CHOL. MG. %	FATTY		TOTAL LIPID MG. %	CA. MG. %	P. MG. %	BLOOD VOLUME		
									ACID MG. %	MG. %				HB. %	C.V. %	PLASMA VOLUME IN C.C.
1934																
3/11	No	--	--	89	32	--	--	--	--	--	--	10.2	2.9	--	--	--
7/11	Yes	96	42	105	32	601	5.8	--	--	--	--	--	--	--	--	--
8/20	No	83	39	108	24	613	6.0	263	316	579	591	--	--	83	39	3855
8/21	Yes	89	40	94	30	601	5.9	250	341	591	591	--	--	89	40	3742
8/30	Yes	86.9	39	92	39	572	6.8	364	678	1042	1042	--	--	--	--	--
12/18	Yes	80	38	86	30	607	7.2	262	663	925	925	--	--	--	--	--
12/19	No	80	38	89	25	607	7.2	258	583	841	841	--	--	--	--	--
(Postpartum)																
1/10/35	Yes	95	42	103	42	601	5.5	308	752	1060	1060	--	--	--	--	--

Various brands of whole posterior lobe pituitary powders were administered by nasal insufflation.<sup>5, 6</sup> Only one of these products proved to be consistently effective. Within a few days it was noted that four to five nasal insufflations daily controlled the thirst and polyuria effectively without any discomfort to the patient due to the treatment.

Soon after the condition was under control, the patient reported complete amenorrhea. The nasal insufflations were not interrupted. Throughout the pregnancy the patient was observed at intervals in the clinic and in the hospital. Blood chemistry, basal metabolism, blood volume, ophthalmoscopic examination, etc., were repeated at intervals with the hope that some pertinent information might be obtained (Table I).

After institution of posterior lobe nasal insufflation therapy, the fluid intake averaged by months was between 3,500 and 2,100 c.c., and the average urinary output was 3,400 to 2,100 c.c. Careful consideration of the daily intake and output record revealed no information of importance, except the return to a normal intake and output when pituitary extracts were administered after temporary cessation of treatment.

No untoward symptoms were noted until Dec. 11, 1934, at about the thirty-seventh week of gestation, when for the first time painful, irregular uterine contractions were noted following insufflation intervals. Not every insufflation was followed by uterine contractions, but the response was more marked as term approached. On Jan. 2, 1935, a normal 3,510 gm. baby was born spontaneously after an eight-hour labor. Absolutely no abnormalities in the character of labor were noted. The child, now two and one-half years old, is perfectly normal.

The patient, two and one-half years after termination of the gestation, is in the same physical condition as she was as soon as posterior lobe medication was begun. The diabetes insipidus is well controlled by posterior lobe pituitary nasal insufflation in approximately the same dosage and frequency of medication as previously.

#### SUMMARY

The history of onset of disease and clinical course is typical of diabetes insipidus.

Physical examination and laboratory findings are all within physiologically normal limits. This includes blood chemistry, blood volume, blood counts, basal metabolism, x-ray studies, ophthalmoscopic examination, and visual fields.

The patient was advised to use the posterior pituitary powder insufflations as liberally as necessary to control the disease. During the last six weeks of pregnancy, it is possible that not quite as much powder was necessary to maintain balance. This observation was entirely subjective and not marked enough to be of importance.

Not until the thirty-seventh week of pregnancy did the uterus respond to the medication by uterine contractions.

The baby, now two and one-half years old, is a normal child.

The patient at the present time requires essentially the same amount of medication as when observed during pregnancy.

The diabetes insipidus apparently was not influenced by the pregnancy.

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## FETAL DEATH DUE TO STRANGULATION DURING LABOR

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THE case herein described is reported because of the unusual findings associated with the death of the fetus.

The patient was a colored multipara of twenty-three years of age. She had had three previous full-term pregnancies, the children all living and well. She was first seen at the Berwind Clinic on Oct. 25, 1933, in the thirtieth week of her fourth pregnancy. The examination was essentially normal and the presentation was thought to be a vertex. The Wassermann reaction was three-plus, although it was negative one month previously. The patient did not return for further examinations.

On November 5, two weeks later, she was seen by a member of the staff because of the onset of labor. The membranes ruptured at 10 A.M. on that day, and the patient was having mild pains which did not continue. The cervix was thick and closed, and the presentation was a breech. After observation it was decided that the patient was in false labor.

True labor began at 8:30 A.M. on November 7, about forty-six hours after the rupture of the membranes. When first seen in her home at 10:10 A.M., the patient was in very strong labor. It was believed that the breech was presenting. The cervix was 6 to 7 cm. dilated and the presenting part was at the spines. No meconium was present. The fetal heart was extremely slow, around 60 per minute. The fetal distress was thought to be due to the strong contractions, and consequently open drop ether was administered. However, twenty minutes later the fetal heart was lost, and labor was progressing rapidly.

Fifteen minutes later the caput presented at the outlet. The head was in R. O. A. position but poorly flexed. It was essentially a bregmatic presentation. As the chin was being delivered, both feet presented at the outlet, just under the chin. There were two loops of cord between the neck and the feet, but these were loose and easily slipped over the shoulders. The baby was then delivered in that position, with the feet delivering with the trunk. The fetal heart failed to respond to attempts at resuscitation.

The baby was a normally developed female weighing 3,000 gm. The lower extremities were flexed at the hips and extended at the knees, so that both feet were under the chin. On the right side of the chin the imprints of the toes could readily be seen. There was congestion of the head and neck, the upper eyelids being swollen with blood. The photograph was taken a few hours after delivery and shows the unusual posture as well as the edema above the neck. At the time of delivery it was felt that death was due to pressure on the neck vessels.

Microscopic examination of the placenta by Dr. H. F. Traut showed leucocytic infiltration of the chorion denoting placentitis and probable infection of the amnion. The villi were not absolutely characteristic although somewhat suggestive of syphilis.

Postmortem examination was done twenty-four hours after delivery by Dr. H. S. Dunning of the Department of Pathology. Except for the edema of the head, the hemorrhages into the upper eyelids, and the imprint of the foot on the

right side of the chin, the external appearance was essentially normal. There were petechiae in the epicardium on the posterior aspect of the base of the heart and in the periosteum of the cranial bones. Numerous ecchymoses were found in the falx cerebri and the tentorium cerebelli, although the tissues were intact. The venous sinuses were normal, but the spinal fluid was blood tinged. The esophagus and the first portion of the jejunum were congested, but the remainder of the gastrointestinal tract was normal. The other organs were essentially normal.

Microscopic examination showed marked congestion of blood in the capillaries and in the small bronchi of the lungs. The alveolar ducts and the alveoli, which were not completely expanded, were filled with particles of amber pigment and a few



Fig. 1.

red blood corpuscles. Some of the pigment was in the cytoplasm of the large mononuclear cells in the alveolar spaces and in the interstitial tissues. The cells of the peribronchial cartilage also contained this pigment.

The spleen showed congestion in the pulp. There were congestion of blood in the capillaries and hemorrhages in the interstitial tissue of the pancreas. The liver also showed marked congestion of blood in the interlobular veins, the sinusoids, and in the central veins, and hemorrhages in the interstitial tissue. In the liver cells there were large drops of pale pink homogenous material. Numerous small collections of nucleated red blood corpuscles were scattered throughout the section. The kidneys showed the same picture of congestion of blood in the cortex and pyramide.

Neurologic examination by Dr. L. D. Stevenson of the Department of Neuro-pathology, was essentially normal except for clotted blood in the subarachnoid

space encapsulating the pole of the right temporal lobe. No abnormalities of the ventricles, basal ganglion, internal capsule, the brain stem, or cerebellum were noted.

The positive pathologic findings were therefore extreme flexion of the lower extremities; hemorrhage into the upper eyelids; congestion of the head and neck; subarachnoid hemorrhage over the pole of right temporal lobe; congestion of lungs, liver, spleen, pancreas, kidneys, esophagus, and jejunum; ecchymoses of falx cerebri and tentorium cerebelli, and petechiae in the epicardium and periosteum of the cranial bones.

#### DISCUSSION

The clinical picture and findings at the time of delivery suggested that death was due to strangulation caused by the pressure of the feet on the neck vessels. The prenatal observations suggested a breech presentation, and this is supported by the unusual posture of the baby at the time of delivery. The pathologic findings are all consistent with this cause of death. Although at the present time there is considerable discussion as to just what the pathologic findings are in cases of strangulation, it is admitted by most pathologists that the findings above mentioned are usually present in those cases. Prematurity may be responsible for the petechiae noted in this case. Although the baby weighed 3,000 gm. and was 55 cm. in length, the presence of nucleated red blood corpuscles in the liver indicated prematurity. The fact that the baby was delivered two months prior to the expected date of confinement supports the diagnosis of prematurity. This of course would accentuate the findings due to strangulation.

Syphilis may have been responsible for the premature labor although the placenta did not show the characteristic findings. The Wassermann reaction was negative six weeks before delivery but was 3-plus four weeks later. (The patient has had two other pregnancies since then. In 1935 she received a course of anti-syphilitic treatment during pregnancy although the Wassermann reaction was plus or minus. A 4,000 gm. baby in good condition was delivered in April, 1935. In May, 1936, she was delivered of a normal 3,400 gm. baby and during that pregnancy the Wassermann reaction was negative.)

Because of the findings, and in the absence of any other definite cause of death, it can be assumed that this mortality was due to strangulation during labor.

From an obstetric point of view this case presents a possibility that might occur with external version. It is surprising that this has not been noted in such cases. This may be due to the fact that the patient had premature rupture of the membranes and that the spontaneous version took place shortly before labor.

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Rosselli, C.: *Dilatation of the Pregnant Uterus, According to the Law of Sfameni*, *Monitore ostet. ginec. (Bologna)* 7: 529, 1935.

The author refers to the writings of Sfameni and others relative to a "diastolic" state of the uterus during pregnancy. He shows that the histologic structure of the wall of the pregnant uterus is not like that of an organ subjected to positive pressure exerted by the growing ovum, as is generally believed, but that of an organ which expands by itself, by a process of active dilatation, a diastole, as Sfameni has asserted for the past thirty years.

AUGUST F. DARO.

## A SIMPLE, SAFE AND ECONOMICAL CORD CLAMP

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MANY types of instruments and appliances have been devised and used to replace ligation in the care of the umbilical cord of the newly born infant. Ligation is still the most commonly used but its popularity is obviously waning. Any successful method must provide complete asepsis, proper hemostasis, and normal wound healing. Several instruments based upon various mechanical principles have been used satisfactorily, some of which have yielded better results than ligatures. Because of the cost of most, if not all, of these instruments, it seemed desirable to make a cheaper clamp equally as effective.

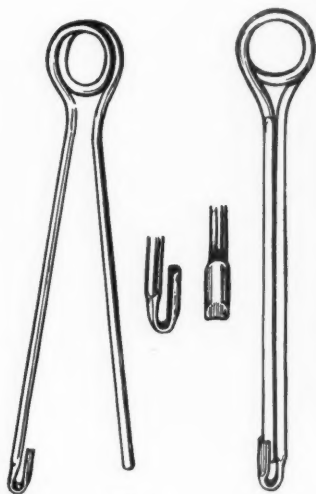


Fig. 1.

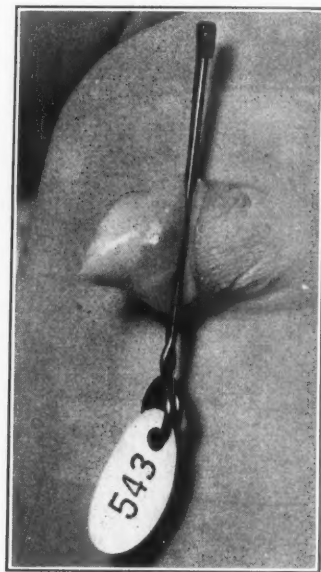


Fig. 2.

Fig. 1.—Perpendicular and horizontal views of the clamp.

Fig. 2.—Appearance immediately after birth with clamp locked in place. Within twenty-four hours the stump will be dry.

Such an apparatus should be safe, be simply constructed, be easily and quickly applied, and allow free inspection without manipulation. These requirements were fulfilled finally in a steel spring clamp. Rectangular strip steel could be substituted but to be equally as strong would have to be heavier and wider.

This clamp is constructed from one continuous piece of wire\* (Fig. 1). The two arms make a direct contact with each other when they are closed, as they have a slight convexity toward each other. One arm is cut longer and bent backward on the proximal side and then grooved in such a fashion that it provides a good catch or lock. The double loop spring portion at the opposite end gives the necessary

\*Mr. Angrabright of the Clinics' Machine Shop made the original models.

flexibility without loss of tension. The two arms are compressed into proper alignment. The various dimensions are as follows: The diameter of the wire 17 to 18 B & S gauge; length over all 6 cm. ( $2\frac{3}{8}$  in.); diameter of the coil spring 1.2 cm. ( $\frac{7}{16}$  in.); the length of the hook or catch 0.4 cm. ( $\frac{3}{8}$  in.); length of arm 4 cm. ( $1\frac{1}{2}$  in.). These dimensions provide ample room for application without contamination, yet the clamp is covered easily by the cord dressing, thus avoiding the dangers encountered with the larger, broader, heavier, and longer instruments.

After clinical tests were made with the "model" clamps and their value was demonstrated, a sufficient number of clamps of stainless steel wire were obtained\* for routine use. Since Nov. 15, 1935, to the present time over 1,500 unselected babies have had their cords treated by this method. Since the systolic blood pressure of newly born infants probably does not exceed 100 mm. mercury and these clamps prevent vascular leaks with pressures in excess of 250 mm. mercury and do not slip, there should be no bleeding. This contention is verified by complete hemostasis in all applications.

The clamp is applied and locked immediately outside the margin of the squamous epithelium. The cord should then be cut 2.0 to 2.5 cm. ( $\frac{3}{4}$  to 1 in.) above the clamp. It is important that this much tissue be left as a margin of safety (Fig. 2). The cord dressing is easily applied. No instrument is used in applying the clamp, and it may remain on until the cord stump falls off. However, if one desires, the clamp may be removed after twenty-four hours. Since it is covered with the dressing, the baby may be turned, moved and handled safely and without risk of injury yet the stump may be inspected at any time by merely removing the dressings. The cord dries promptly and usually drops off in three to seven days. Furthermore the healing process has not only been enhanced but also has been extremely satisfactory.

These stainless steel clamps have been used repeatedly without showing loss of quality. They are simple, safe, dependable, and very economical.

A more detailed report will be made later.

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\*The American Spring Coil Company, Muskegon, Michigan, made these clamps.



## Special Article

HUGH LENOX HODGE

A MASTER MIND IN OBSTETRICAL SCIENCE

HERBERT THOMS, M.D., NEW HAVEN, CONN.

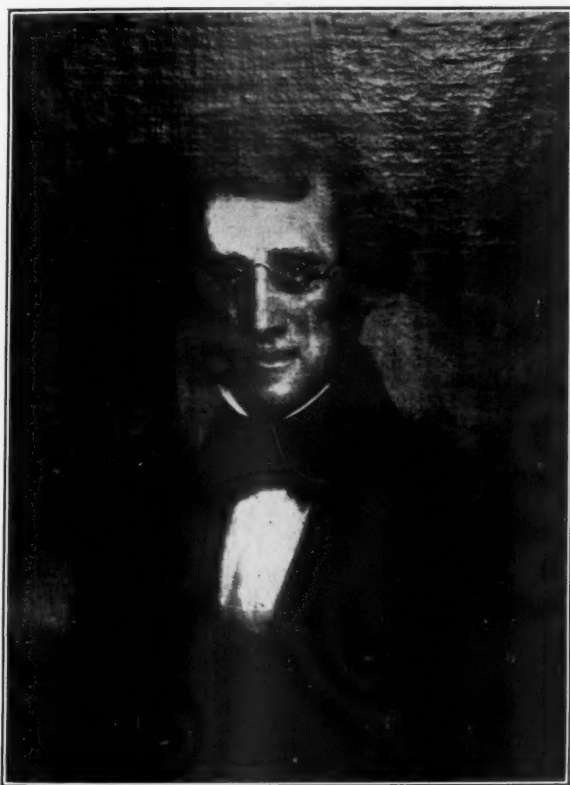
MEDICAL textbooks of a former generation for the most part are interesting only from the historical point of view. There are exceptions, however, for rarely we find among these faded volumes one which is so masterful in its delineation, so fraught with the truths of experience that we are able to view in clearer relief the real stature of a great mind of other days. Such a work is *The Principles and Practice of Obstetrics* by Hugh Lenox Hodge, published in Philadelphia nearly three-quarters of a century ago. Hodge's work is the true progenitor of our modern American textbooks on this subject. Indeed, many of its fine lithographic illustrations have not been equalled, and much of its facility and clarity of description has not been surpassed. "This volume," wrote Whitridge Williams, "which is a model of conscientious observation, is undoubtedly the most original work which has appeared in America, and with few modifications is as valuable today as when first written."

If we review the history of obstetrics in our country during the middle years of the last century, eminence seems to center around two names, Charles D. Meigs and Hugh L. Hodge, both of Philadelphia. These two leaders in medicine were unrivaled in their influence as teachers of obstetrics, and although the former was probably the more spectacular personality, the contributions of the latter evince a soundness and originality that we are more prone to associate with true greatness.

Hugh Lenox Hodge was a descendant of Andrew Hodge, a Scotch-Irish Presbyterian who emigrated to America in 1730. With two brothers he settled in Philadelphia, entering the mercantile business. A son of Andrew Hodge and father of Hugh Lenox Hodge, was Hugh Hodge, born in 1755 and graduated from Princeton College in 1773. Shortly after this he was apprenticed in medicine to Thomas Cadwalader, a noted physician and one of the first lecturers on anatomy in the new world. During the Revolution Dr. Hugh Hodge became an army surgeon, was captured by the British and liberated on parole through the intercession of General Washington. After the war he settled in Philadelphia and in 1790 married Mary Blanchard of Boston. Hugh Hodge

played a prominent part in the terrible epidemic of yellow fever in 1793 and 1795, and it is probable that his labors at that time hastened his early death in 1798.

Hugh Lenox Hodge was born in Philadelphia, June 27, 1796. His early education was gained under Mr. Thompson at the grammar school of the University of Pennsylvania and later at boarding schools in Summerville and New Brunswick, New Jersey. At the age of fifteen years he entered the sophomore class at Nassau Hall, Princeton. Here at this



HUGH LENOX HODGE

time also as a student was his only brother, and in order to defray expenses the mother moved to Princeton and took four other students into her family.

In September, 1814, Hodge graduated and immediately began the study of medicine in Philadelphia under the celebrated Caspar Wistar, then at the height of his fame. In August, 1818, at the age of twenty-two he was graduated a doctor of medicine from the University of Pennsylvania. At this time it was his desire to spend a year of study in Europe, and following the footsteps of his teacher T. C. James he enlisted as a ship surgeon on a vessel bound for Calcutta. He sailed from

New York on the "Julius Caesar" on Sept. 8, 1818, and five months later arrived in India. Unlike his preceptor, however, the voyage was a financial failure although his rich experience in the cholera hospitals at that time was to stand him in good stead during the cholera epidemic in Philadelphia in 1832. On his return to America he opened an office on Walnut Street and soon after was elected physician to the Southern Dispensary and to the Philadelphia Dispensary. In the summer of 1821 he was selected to teach the anatomy class of William E. Horner who was absent in Europe. Two years later he was appointed to the lectureship on Surgery in Chapman's summer school, which later became the "Medical Institute." This last appointment says Hodge was a turning point in his life and led him into medical teaching as a career. Not long after this an unexpected change in his career took place. Because of a gradual failure in vision he was led to abandon surgery and turn his attention to another field. He chose obstetrics.

In 1828 Hodge married Margaret Aspinwall, the daughter of John Aspinwall, Sr., of Flushing, New York. To them were born seven sons, four of whom became clergymen and one who became a surgeon.

When Thomas Chalkley James resigned his Professorship in Obstetrics at the University of Pennsylvania in 1834, William Potts Dewees was chosen his successor. However, because of ill health the latter was forced to withdraw and the chair became vacant. The leading candidates for the position were Hugh L. Hodge and Charles D. Meigs. In his innate modesty Hodge refused to exert himself for the position, much to the annoyance of friends who were working for him. The young candidate was finally prevailed upon to call upon the trustees. At his first visit to a very eccentric friend, after stating his errand he was told "young man, I should have thought better of thee, hadst thou not come." This was the first and last visit of that nature that Hodge made. Nevertheless his friends continued to work and the campaign, for such it was, resulted in his election. He now joined the medical faculty with Nathaniel Chapman, Robert Hare, William Gibson, William E. Horner, Samuel Jackson, and George B. Wood.

His first term in the chair was not an unmixed blessing, for it was customary for the new professor to pay the trustees an entrance fee of \$600, and furthermore these gentlemen had promised Dewees that the proceeds of the course after expenses had been deducted should revert to him. However, Hodge's connection with the University soon brought him a lucrative practice, patients coming from great distances, particularly from the Southern States.

His vision which had insidiously failed by 1850 had become so impaired that he was unable to read ordinary written manuscripts. Ten years later when his volume *Diseases Peculiar to Women* was published, it proved to be the last effort made with his pen. In addition to this affliction, the years of the Civil War showed a great diminution in his

practice particularly among his Southern clientele. Following his course in 1862 and 1863 because of failure of vision he resigned his professorship and became emeritus. He now devoted his time to the writing of his great work the *Principles and Practice of Obstetrics* and in producing this he had to rely on an amanuensis and on editorial assistance from his son.

From the professional viewpoint the remainder of Hodge's life does not have peculiar interest. A biographer says "sixty-seven years old, he did all the professional work which could be done without eyes. The poor and the students could still count upon finding him in a serene mind, tender and sympathetic with a loyal unswerving trust in God." In 1871 his Alma Mater in medicine honored herself and him by bestowing the degree of Doctor of Laws and in 1873 on February 23 after a day's illness with cardiac failure he passed on.

The outstanding and important contributions of Hugh Lenox Hodge are found in his *Diseases Peculiar to Women* (1860) and *The Principles and Practice of Obstetrics* (1864). In the former is found an excellent description of the appliance which added greatly to his fame, the well-known Hodge pessary. The evolution of this instrument was the result of many years of experimentation during which countless shapes were tried and many materials used. Hodge was one of the first to use vulcanite after its invention by the pioneer Goodyear. The important modification introduced by him consisted in making the ring oblong instead of circular and so curved as to correspond to the curvature of the vagina. During the period of the evolution of this instrument, a biographer writes, "Sitting one evening in the University his eyes rested on the upright steel support designed to hold the shovel and tongs, which were kept in position by a steel hook, and as he studied its supporting curve, the longed-for illumination came and the lever pessary was the result." In order to evaluate the importance of this mechanical device as a boon to suffering womankind, we must remind ourselves that plastic surgery for female ills was in Hodge's day practically unknown.

Hodge's great contribution to medical literature was his *Principles and Practice* first published in 1864. Because of necessary space limitation, we can but figuratively glance into the pages at this time, but even this will give some idea of the true greatness of his contribution to obstetrics. The fine historical essay in the preface shows the author's familiarity with the authors of his day and with those who have gone before. Under "anatomy of the pelvis" he gives a fine description of his theory of parallel pelvic planes which, though of little practical use today, does show how familiar the author was with the architecture of the pelvis. Hodge was even familiar with variations in this architecture and their influence on labor as is witnessed in the following quotation. Under "occipito-pelvic position" he writes, "In this position (the third of Baudeloque) the occiput is toward the pubis and the superior part of the os points

toward the lumbar vertebrae, of course the spine and back are directly anterior . . . in a few cases, the continuance of the third position may be maintained by some peculiar elongated form of the superior strait, so that the anteroposterior diameter may be comparatively long."

At a time when cesarean section was almost universally condemned, Hodge's view had a real prophetic note; he writes, "The hope, also, may be entertained that if the patient be in good condition mentally and physically, and if the deformity of the pelvis be ascertained previous to the recurrence of labor, so that suitable preparations can be made for the operation, gastrohysterotomy will prove far more successful than in times past, and, perhaps may be justified even in cases of moderate deformity, when the child is alive, for the purpose of preserving its life as well as that of its mother."

There is no doubt that Hodge was an outstanding authority in deformities of the pelvis and his evaluation of external pelvimetry as a method of diagnosis sounds indeed a modern note as witnessed by the following: "Many physicians have placed great confidence in the external measurements of the pelvis; but this is liable to many errors, even from the varying conditions of external tissues, and can in no sense give any exact idea of the form or dimensions of the pelvic cavity."

Hodge opposed Holmes' views with regard to the contagiousness of puerperal fever, but unlike his vehement colleague, Meigs, he raised no animosity in the heart of the young professor at Harvard. "His remarks," Holmes observed, "are unobjectionable in tone and language, and may be read without offence." In Hodge's *Principles and Practice* the whole subject of childbed fever is treated in a minimal way and no reference is made to the controversy which had raged a dozen years prior to its publication. Hodge is said to have been opposed to anesthesia in childbirth but this is an error. He was apprehensive of the use of chloroform, but his words on the subject of anesthesia show him to be essentially an advocate of its use. His views are summed up in the following quotation:

Often a slight anaesthetic influence may be sufficient to moderate without destroying sensibility, so that labor progresses regularly, without any considerable pain or disturbance. This is all that is necessary, except in a few, perhaps very few, obstetric operations. The author, therefore, coincides in belief with those who insist that the patient ought not to be entirely unconscious. The practitioner should have command of his patient, that he may direct what sensations are to be resisted, and what should be encouraged; when the bearing-down efforts are desirable, and when they should be remitted; and, of course, the woman should be in a condition to advise her attendant as to the occurrence of any unusual pain, morbid sensation, etc. There are a few cases of course, where complete anaesthesia may be essential.

In describing the conduct of the third stage of labor, Hodge anticipated the maneuver that we associate with the name of Credé, he



writes, "Should there be any unusual delay, the practitioner may facilitate the contraction of the uterus by placing his hand through the medium of the relaxed walls of the abdomen, over the fundus of the uterus, and by making firm pressure direct the whole organ towards the superior aperture of the pelvis."

How well Hodge anticipated many of our modern views with regard to labor mechanism is shown by the following. "In describing the mechanism of labor, it will be found that the head of the infant descends from the superior strait to the floor of the pelvis very nearly in a straight direction, corresponding to the axis of the superior strait. The top of the head which was originally parallel to the superior strait, does not materially alter its direction until it comes in contact with the coccygeal region. It will be found also that the important process termed extension does not commence until the descent just mentioned, be nearly completed; indeed that it cannot occur until the top of the head reaches the perineum, and the suboccipital region passes under the arch of the pelvis."

Hodge was a great believer in the forceps and wrote, "A very large proportion of the vesico-vaginal fistulae, too frequently to be met with, result, *not from the use, but from the neglect of the forceps.*" His own modification of this instrument embodied many advantages over most of the instruments of his day; his endeavor was to "embrace all the advantages, without the defects of the Baudeloque forceps." His directions concerning the forceps may be quoted as a model of instruction.

Second rule to be observed is, to operate very slowly, and in the direction of the axis of the pelvis. The object of the accoucheur is to imitate nature as far as practicable; in spontaneous deliveries, in contracted pelves, labor is necessarily tedious; the compression to which the head is subjected is always gradual allowing time for the yielding of the commissures, the overlapping of the bones, the elongation of the head, and the consequent alteration of the form of the contour of the cranium. Hence, the forceps being applied, very slight compression and traction should be made at first; the patient should be encouraged to make her bearing down efforts, and the practitioner should afford moderate assistance during the existence of a pain. As soon as this intermits, pressure should be removed from the handles, so as to free the head as much as possible from compression. . . . It should never be forgotten that the forceps should be regarded as a mere addition or substitute for the natural powers by which the child is expelled.

In conclusion, the following quotation from his chapter on labor is significant of the soundness and truth of his doctrines.

These observations, the truth of which must be palpable, justify the declaration, that every labor should be under the supervision of a scientific accoucheur, in order that there may be no interference, direct or indirect, with the natural process of delivery. It is the business, therefore, of the practitioner carefully to watch the whole process of labor, to ascertain whether it is perfectly regular, and to detect any, even the least deviation from the natural process, that timely assistance may be rendered.

The foregoing excerpts from Hodge's important treatise bear out the statement of Williams as to its value as a fundamental work of reference. The real inquiring student today should not overlook the many practical suggestions to be found therein. Perusal of its pages reveals the writer as a master of his subject, but there is other and perhaps finer inspiration to be gained from Hugh Lenox Hodge than one finds in his written word. The fine fortitude which he displayed in carrying on his life work under his terrible affliction shows his true greatness. His life exemplified those qualities which we associate with mastery of life and superiority among men.

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Maternity care propaganda to be helpful must be conducted on lines of reassurance and not of menace. The susceptible nervous system of the pregnant woman is readily impressed by a recital of possible complications even to the extent of what has been termed anxiety neurosis.

An essential objective to ensure the success of maternity services is to gain the confidence and support of women generally. The postnatal care should be the corollary of the antenatal clinic, in view of the fact that 40 per cent of the cases attending gynecologic out-patient departments have a causal relation to obstetrics.

The midwife may make or mar the success of any maternity service.

A national maternity service which excludes the general practitioner from its responsible personnel is impossible and unthinkable. The consultant is essential to a maternity service. He consults with the general practitioner.

The hospital is an indispensable adjunct of a maternity service, provided the maternity beds are kept well separated from the mixed hospital. The home is infinitely safer than the carelessly conducted hospital. The availability of analgesia or anesthesia for parturient women is a factor in gradually increasing numbers applying for institutional care. The conduct of and the equipment for home deliveries will remain the center of the whole problem and will, in the main, control the mortality and morbidity rates.

For a national service both central and local advisory bodies with suitably representative membership and with responsible status would be necessary.

F. L. ADAIR AND S. A. PEARL

# Department of Practical Problems in Obstetrics and Gynecology

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CONDUCTED BY WILLIAM J. DIECKMANN, M.D.

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## IRRADIATION OF MALIGNANT DISEASES OF THE FEMALE GENITALS

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THE introduction of radium and roentgen rays for the treatment of malignant disease has found widespread application in lesions of the female generative tract. The success of these agents has led unfortunately to their abuse in many instances, and it is essential not only that a study be made of the indications presented by each patient but that a definite knowledge be acquired of the manifold effects and complications which attend their employment.

In the treatment of malignant or suspected lesions, a biopsy is necessary before radiation is administered. Removal of a small piece of tissue from a suspicious lesion of the cervix rarely produces bleeding that cannot be controlled easily. Curettage should be performed in all cases of abnormal bleeding from the uterus. A more formidable operative procedure may be required for obtaining a biopsy specimen in cases of ovarian tumors, or other deep-seated lesions. The histologic appearance of a tumor may have an important bearing upon the method of treatment, as well as the prognosis. Some lesions may be treated best by surgery alone. For others radiation may be the method of choice. In many instances both radiation and surgery are employed.

### CARCINOMA OF THE CERVIX

Carcinoma of the cervix is a disease that may be considered as moderately radiosensitive. In most clinics surgery has been abandoned for patients with that disease, and treatment is given by radiation alone. The degree of radiosensitivity is difficult to determine, due chiefly to the destructive doses generally employed. However, there is evidence that at least 6 to 8 threshold doses must be distributed throughout the primary lesion to control the disease in that region.<sup>1, 2</sup> Radium applied to the uterus alone will not deliver a lethal dose to points located at distances greater than 3 or 4 cm. from the cervical canal. This has been shown diagrammatically by charts illustrating the distribution of radiation for different methods of applying radium to the cervix.<sup>3</sup> No single method is suitable for the treatment of all patients, and in some instances it may be impossible to make a satisfactory application of radium. The most suitable distribution of radiation will be obtained from an intra-uterine tandem combined, whenever possible, with some method for delivering radiation into the vaginal fornices lateral to the cervix. The so-called colpostat is used most frequently for that purpose.

Some means other than radium applied to the cervix must be employed in the attempt to treat adequately the outlying tumor-bearing regions, such as external irradiation by roentgen rays. Taussig<sup>4</sup> performs lymphadenectomy after irradiation, or at the time radium is used. The radium treatment consists of a cervical application, or the insertion of gold seeds into the regions occupied by the various lymph glands. In some instances both methods may be employed. The best results have been obtained in Group II patients (*League of Nations Classification*), to whom that procedure is now limited.

The amount of external irradiation that must be delivered in the attempt to treat adequately the disease in the outlying tumor-bearing regions will produce an erythema of a rather marked degree in the irradiated skin fields, and some constitutional reaction in the patients receiving the dose. Due to the fact that the parametrial regions and the adjacent lymph glands are involved in most instances, the administration of roentgen rays is just as essential as the application of radium to the cervix. It is important, therefore, that the tissue damage at the site of the application of radium be limited to a degree that will not interfere with the administration of external irradiation. The use of x-rays in conjunction with radium applied to the cervix delivers greater doses to points throughout the pelvis than could be obtained from either method alone. By this means the volume of tissue receiving a lethal dose will be increased, whatever the method of applying radium to the cervix. The degree of increase will depend upon the amount of roentgen radiation reaching the tumor.

There are certain advantages to be gained if the treatment of a cervix case is begun with x-rays. By this means any existing infection will be diminished, which, in turn, will reduce the degree of reaction and the incidence of complications from the radium treatment given at a later date. Furthermore, the application of radium may be facilitated by regression of the size of the primary lesion.

Roentgen treatment can be administered in single exposures to each pelvic field, or a divided dose technic may be used. The latter procedure is not always practical for patients who have very advanced disease, and a marked amount of pelvic inflammation. For the average patient it has been found that from 2,000 to 2,400 roentgens (measured in air) can be delivered safely to each of four areas (2 fields on the anterior surface of the pelvis, and 2 on the posterior), if administered over a period of from twenty to thirty days.<sup>5</sup> A six-field technic (2 on the anterior surface, 2 on the posterior, and 1 on each lateral aspect of the pelvis), with a 70 cm. target-skin distance, has been found to deliver a distribution of radiation that is best suited to the treatment of cervix cancer.<sup>6</sup> If six fields are irradiated it may be necessary in some instances to reduce the total dose given each area to 1,500 roentgens, when the treatment is administered within a period of about three weeks.<sup>7</sup> In the average patient each method will deliver from 2 to 3 threshold doses throughout the tumor-bearing region. The administration of large amounts of external irradiation is particularly important in the treatment of carcinoma of the cervical stump.<sup>2</sup> In the absence of the uterine corpus it is difficult to make a satisfactory application of radium.

It is essential that patients be observed at frequent intervals during a course of divided dose treatment. The regression of the primary lesion should be observed carefully. In some instances, due to the marked shrinking and stenosis of the cervical canal, it may be necessary to

interrupt the external irradiation and apply radium. The reappearance of actively growing tumor noted in serial biopsies taken within the first two weeks following roentgen treatment indicates that, whenever possible, radium should be applied within that period.<sup>1</sup>

The average intrauterine tandem used in the treatment of cervix cancer consists of 2 capsules. The strength of the lower capsule (cervical portion) is usually about twice that of the upper one. The tandem should be applied so that it is surrounded completely by the cervix with the lower end about level with the external os, or the most dependent portion of the primary lesion. Various intravaginal applicators can be used also, depending upon the gross character of the lesion in question. After the application the vagina is distended with gauze packing to increase the distance of the bladder and rectum from the radium in order to protect those structures from excessive doses. An indwelling catheter can be used to keep the bladder collapsed so that it will receive a minimum of exposure.

The full amount of the radium treatment may be administered by means of a single application, or, as was noted for x-rays, the total dose may be divided into several treatments given a few days apart. For a number of years Healy<sup>2, 8, 9</sup> has delivered the full amount of radium radiation within thirty-six to forty-eight hours. He believes that an intrauterine tandem should not be left in place for periods longer than twenty-four hours without being removed and cleaned. Due to the presence of bacteria, prolonged applications may lead to complications from infection. Radium is applied within seven to ten days after the completion of a cycle of external irradiation. One of several intravaginal applicators, usually the so-called bomb, is directed toward the cervix, or into the lateral vaginal fornices for doses of 1,500 mg. hr. in each position. Due to excessive reactions he has, during the past few years, employed the intravaginal applicator in one position only, which is usually against the cervix. On the following day a tandem is inserted into the uterus for a dose of 3,000 mg. hr. The tandem is of sufficient strength to deliver that amount of radiation within about twenty-four hours. Six weeks after the radium treatment the cycle of x-rays is repeated, unless a divided dose technic had been employed for delivering a large amount of roentgen radiation before the application of radium.

At the Radiumhemmet (Stockholm) the radium treatment is divided usually into three applications. The first two are separated by an interval of one week, and the last is given three weeks later. Complete treatment, therefore, requires about four weeks. Heyman<sup>10</sup> uses a tandem in combination with various cylindrical or flat intravaginal applicators. At each treatment the average dose for the tandem is 800 mg. hr., and for the intravaginal applicator is 1,500 mg. hr. After complete treatment about 2,400 mg. hr. will have been delivered by the tandem, and about 4,500 mg. hr. by an intravaginal applicator. For a number of years external irradiation was not employed in every instance. Since 1929 all patients with cervix cancer have received roentgen or telerradium radiation. Heyman states that the combined treatment has resulted in an improvement in results over those obtained from radium applied to the cervix alone.

It is interesting to note that the various technics employed for applying radium to the cervix at the Memorial Hospital (Healy), the Radiumhemmet (Heyman), and at other institutions, have produced about equal clinical results. The absolute five-year cure rates have ranged from



20 to 22 per cent. (For carcinoma of the cervical stump the cure rate is only about 14 per cent.<sup>2</sup>) It is agreed generally that advance in the treatment of cervix cancer will be made by improving the methods for administering external irradiation, rather than by changes in technics for applying radium to the primary lesion.\*

Schmitz<sup>11</sup> has published statistics showing an improvement in results for the changes made in his technic of irradiation over the past twenty years. The absolute curability for gynecologic carcinomas was given for various periods during which particular methods and specified doses were used. For the most part the changes were related to the administration of roentgen radiation. The first improvement in results was noted after 1921 when he began to use 200 kv. x-rays. There was no change in the radium dose of 3,000 mg. hr., which was administered by a single application. The second improvement in results occurred after 1926, when a divided dose technic was begun. The patients were irradiated through 2 to 4 skin fields until 1,375 to 1,800 roentgens had been delivered to each area. In some instances the radium dose was increased to 4,800 mg. hr., which was administered in three applications of 1,600 mg. hr. each that were given at intervals of eight days. Since 1933, he has used voltages ranging from 500 to 800 kv. Treatment has been administered by fractionated doses through 2 or 3 skin fields until 3,000 roentgens were delivered to each area. It is interesting to note that since the use of voltages of that order, he has decreased the radium dose to 1,200 mg. hr., and in some instances radium treatment has been omitted. The present method has not been in use for a time sufficient to permit observation of the results over a five-year period. However, he compared the preliminary results obtained within eighteen to thirty months after irradiation for all of the methods. Those values indicate that the results from the present technic will show improvement over those obtained from preceding ones. The improved results from external irradiation cannot be attributed to a change in quality alone. There has been a definite increase in the total dose delivered to each field, as well as in the amount reaching the tumor. Schmitz states that the value of 800 kv. x-rays can be determined only when the percentage of five-year cures is known. He adds that both radium and 200 kv. x-rays have proved to be of definite value, and will continue to be used. The greater voltage may be indicated in the treatment of large deep-seated lesions that cannot be irradiated adequately by the methods used most frequently at the present time.

#### CARCINOMA OF THE CORPUS

Surgery has proved to be an efficient method of treatment for early cases of corpus cancer. However, all patients with operable lesions cannot be treated by hysterectomy, because the disease tends to occur in elderly women. Age alone may not contraindicate an operative procedure, but there are frequently associated conditions that increase the risk considerably. Furthermore, there is evidence that hysterectomy

\*It should be noted that no mention has been made of the use of interstitial irradiation (seeds, needles, etc.) in the treatment of cervix cancer. Methods employing interstitial sources have not been employed generally, but Ward and others have for a number of years used needles inserted into the cervix in conjunction with an intrauterine tandem. Since this paper was written there appeared a publication by Pitts and Waterman (*Surg. Gynec. Obst.* 64: 30, 1937). They used weak needles several centimeters in length implanted into the paracervical and parametrial tissues (in conjunction with an intrauterine tandem) for large doses delivered at low intensities over periods of five days or longer. Their five-year statistics are probably the best that have been obtained for cervix cancer in this country.

alone is inadequate for all patients with operable lesions. It has been demonstrated that a definite relationship exists between the histologic structure of the tumor and the end-results.<sup>12-14</sup> In the well-differentiated lesions a high percentage of cures has been obtained. Practically none of the patients with anaplastic varieties of carcinoma have survived if treated by surgery alone.

The influence of the histologic type upon the prognosis, and the large number of patients not suited to surgery due to associated constitutional conditions, have led to a greater use of radiation in the treatment of corpus cancer. Some authors advocate radium and x-rays for all cases of this disease.

For evaluating surgery and radiation several reports<sup>15</sup> have been published showing a comparison of the average five-year results in collected statistics. For all cases treated by irradiation, including both operable and inoperable lesions, cure rates of from 32 to 36 per cent have been shown. Among patients with operable lesions, from 47 to 54 per cent have survived the five-year period. In every large series the cures from hysterectomy have been from 56 to 59 per cent. It is interesting to note that among patients who might be considered suitable for surgical treatment, Heyman<sup>10</sup> has reported a relative cure rate of 64.3 per cent for irradiation alone.

It is not essential that all patients be treated by only one method. In many clinics both radiation and surgery are combined in some instances. Postoperative irradiation has been used extensively. Preoperative treatment has been employed less frequently, and it is feared by many that the use of x-rays or radium would increase the technical difficulties of an operation performed at a later date. This has not been the experience of Healy.<sup>16, 17</sup> He compared the effect of radiation administered before and after hysterectomy in 24 patients with adenocarcinoma, Grade 3. Fifteen of the patients were irradiated before the uterus was removed. Of this number 60 per cent were cured. In 9 patients postoperative treatment was given, and only 33 per cent survived. It should be noted that most of the patients who were treated before operation received an intrauterine application of radium in addition to x-rays. Those who were given postoperative irradiation were treated by means of roentgen rays alone.

In a collected series of 91 patients who received an intrauterine application of radium before hysterectomy, 60 per cent were reported as cured.<sup>15</sup> These results indicate that the combined method of treatment is to be advocated, whenever practical, for all patients. It is particularly important in those with undifferentiated tumors. Radiation alone may prove to be the best procedure in such instances. That will be decided after a large number of patients suited to surgery have been observed in clinics treating all cases of corpus cancer by irradiation.

In the radium treatment of corpus lesions it is difficult to determine the size and location of the tumor. The disease may form a bulky mass that will distort the cavity so greatly that radium cannot be applied in a manner that will deliver a suitable distribution of radiation. Approximately 20 per cent of the cases are complicated with myomas that may also distort the cavity. Sampson<sup>18</sup> has demonstrated those difficulties by means of radiographs taken of removed uteri into which had been placed capsules to simulate the radium treatment of corpus cancer. He also discussed the danger of the radium capsule acting as a piston to force blood containing tumor cells through the lumina of the

tubes into the peritoneal cavity. There is also the danger of perforating the uterine wall if pressure is made during the insertion of radium against a portion of the myometrium that is infiltrated by the disease.

To begin treatment with a course of x-rays would seem to be equally applicable to corpus cases as to cervical lesions. Among patients with bulky tumors distorting the cavity so greatly that a suitable application of radium cannot be made, a preliminary course of x-rays will facilitate the intrauterine treatment by reducing the size of the lesion. Furthermore, the danger of forcing viable cancer cells through the lumina of the tubes should be reduced. The combination of x-rays and radium will deliver greater doses to points throughout the pelvis than could be obtained from either method alone. In patients who are not to be operated upon, a more marked effect may be obtained from the external irradiation if a divided dose technic is used. If hysterectomy is to be performed, it seems desirable to limit the roentgen treatment to single exposures to each pelvic field.

For the radium treatment the active length of the intrauterine application should extend from the external os to the top of the fundus. The volume of tissue that will receive a lethal dose from a tandem (capsules end to end in a straight line) is not great. This has been shown histologically by the irregularities in radiation effect noted in various portions of the same uterus.<sup>15</sup> Any method that will distribute the radium more widely throughout the cavity will improve the distribution of radiation. Hurdon and Chambers,<sup>19</sup> Held,<sup>20</sup> and others have published diagrams showing the probable zone of effect for several methods of inserting radium into the uterus. Dietel<sup>21</sup> has devised an intrauterine applicator by means of which capsules within the cavity can be arranged in a triangle, or in a so-called "bouquet." Heyman<sup>10</sup> fills the uterine cavity with containers of various sizes that hold radium sources. Schmitz<sup>22</sup> uses an adjustable "Y"-shaped applicator.

The average dose of radium employed in the treatment of corpus cancer ranges from 3,500 to 4,500 mg. hr. The application may be made during the first two weeks following external irradiation. For a number of years, Healy<sup>16, 17</sup> has employed both radium and x-rays in many patients before the uterus was removed six to eight weeks later. In more than 50 per cent of the removed uteri, there was no evidence of viable cancer. If there is a possibility that some portions of the disease have not been irradiated adequately, hysterectomy should be performed, whenever practical, before recovery has taken place. Cellular alterations of the tumor appear within a few weeks. Additional data may indicate the time at which the maximum radiation effect is produced, and the rate at which the tumor recovers from a sublethal dose. The optimum time for hysterectomy would be after the greatest degree of radiation change, and before there was recovery from inadequate doses.

#### CARCINOMA OF THE EXTERNAL GENITALIA

The malignant lesions of the external genitalia are chiefly epidermoid carcinomas of an adult type that are relatively radioresistant. The disease tends to occur in elderly women among whom the tissues about the vulva are easily damaged, and usually show abnormal changes that are already present. Those regions will not tolerate the amounts of radiation required in most instances. As a result, the use of radiation has usually been limited to patients who were inoperable due either to the extent of the disease or some associated constitutional condition.

The results have not been satisfactory. It should be noted that the age incidence of vulval cancer is so high that many patients die of intercurrent disease before the five-year period has elapsed.

For the double-sided Basset operation, Taussig<sup>23</sup> reports an operability of 75 per cent, and a primary mortality of only 4.6 per cent. In a series of 23 patients treated by that method he obtained a five-year cure rate of 65 per cent, and among 12 patients 55 per cent survived ten years. Those statistics are probably among the best that have been given for vulval cancer.

Healy<sup>16</sup> states that among 8 patients who survived the five- to ten-year period, surgical removal of the vulva, and dissection of one or both groins was the important procedure in each instance. However, all of the enlarged inguinal glands were not infiltrated by the disease. He feels that dissection of the groins is not essential in every instance. For some time he has omitted radiation in the treatment of the primary lesion, which is removed by complete vulvectomy. The groins are treated with x-rays. If nodes appear in those regions, they are exposed and gold seeds implanted so as to deliver not less than 5 threshold doses.

#### CARCINOMA OF THE VAGINA

Carcinoma of the vagina has been cured rarely by surgery alone. For radiation Healy<sup>16</sup> reports a five-year cure rate of 12 per cent. In 129 irradiated cases he cited from the literature, 12.4 per cent survived that period. The soft, friable, vascular lesions of the cauliflower variety usually show the greatest response to radiation. Only palliative results can be obtained in the large annular lesions filling the vagina. Fistulas into the bladder or rectum are fairly common sequelae, if the primary lesion is located in the vesicovaginal or rectovaginal septum.

Treatment should be given with both x-rays and radium. A protracted roentgen treatment with multiple exposures totaling 1,500 to 2,000 roentgens to each area will usually produce considerable regression in the size of the lesion. Following this procedure various plaques, or other intravaginal applicators containing radium, can be used at distances of about 1.0 cm. for doses ranging from 1,000 to 2,000 mg. hr. The total amount of radiation delivered to the diseased area can be increased if it is practical to use interstitial sources of radium in addition to the above methods.

#### OVARIAN TUMORS

Ovarian tumors present a wide variety of histologic types, some of which respond to radiation, while others remain relatively unaffected. A favorable response has been noted rather consistently in those that contain calcium deposits in the form of psammoma bodies. Practically all of the embryonal carcinomas, and other undifferentiated types are radiosensitive. However, biopsy is difficult to obtain, and the variety of tumor in question is not known usually until after operation. In some instances tissue for histologic diagnosis has been obtained by cul-de-sac puncture.

Whenever practical the patients are usually treated surgically. Tumors that prove to be malignant are given postoperative irradiation. Healy<sup>16</sup> states that the five-year cures from surgery vary from 10 to 15 per cent.

If for various reasons the tumor cannot be treated surgically, all large amounts of fluid present in the abdomen or in cysts of the tumor



should be removed before irradiation. In some instances tumors may disappear, or decrease in size so that they can be removed at a later date.

For irradiating ovarian tumors the entire abdomen should be included. It is usually necessary to employ upper and lower abdominal areas on both the anterior and posterior surfaces. The operative scar should be included in the direct beam, due to the frequency of recurrences in that region from implantation metastases. Complete treatment will usually require from two to three weeks. During that time from 1,000 to 1,500 roentgens can be delivered to each area.

#### CARE OF THE IRRADIATED PATIENT

It is desirable, whenever possible, to keep patients ambulatory and reasonably active during a course of roentgen treatment. The presence of an abdominal dressing does not interfere materially with the administration of external irradiation. However, it is essential that all adhesive tape be removed from the *skin fields*, and that the tape never be replaced to those areas after treatment. This is necessary because the presence of adhesive will in every instance increase the reaction in the underlying skin. Mild irritation of the irradiated fields can be treated with any bland skin lotion. If ulceration occurs, then vaseline or olive oil dressings give greater relief.

Intestinal irritation from x-rays or radium can be diminished usually by regulating the diet, and the use of opiates, etc. The discomfort from severe proctitis may be relieved by injecting several times a day a few cubic centimeters of warm oil, or the insertion of suppositories containing some anesthetic. Mixtures containing tinctures of belladonna and hyoseyamus are useful in the treatment of cystitis. Every patient should receive daily a vaginal douche of some antiseptic solution, such as potassium permanganate (1:1,000).

The amount of radiation required for the treatment of malignant diseases of the reproductive system may produce some anemia and leucopenia. Various medications and sedatives that may have a damaging effect upon blood cells should be avoided.

Patients should be observed at frequent intervals during their convalescence following irradiation. It is essential that all patients with malignant disease be followed carefully by regular and periodic examinations, so that any complication, or recurrence of the disease, will be recognized at the earliest time possible.

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## Society Transactions

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### NEW YORK OBSTETRICAL SOCIETY

*MEETING OF OCTOBER 13, 1936*

The following papers were presented:

**Extraperitoneal (Latzko) Cesarean Section.** Dr. Albert H. Aldridge. (For original article, see page 788.)

**The Endocrine Basis of Toxemia of Pregnancy.** Drs. J. J. Vorzimer, E. G. Langrock, A. M. Fishberg, and E. M. Rappaport. (For original article, see page 801.)

*MEETING OF NOVEMBER 10, 1936*

The following paper was presented:

**A Study of Dermoid Cysts With a Suggestion as to the Use of X-ray in Diagnosis.** Dr. Morris Glass and Dr. Alexander H. Rosenthal. (By invitation.) (For original article, see page 813.)

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### OBSTETRICAL SOCIETY OF PHILADELPHIA

*MEETING OF NOVEMBER 5, 1936*

The following papers were presented:

**On Certain Pharmacologic Actions of the Newer Barbituric Acid Compounds.** Dr. Charles M. Gruber. (For original article, see page 729.)

**Analgesia With the Barbituric Acid Derivatives and Its Relationship to Sudden Death in Labor.** Dr. Thaddeus L. Montgomery. (For original article, see page 745.)

# Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D.

## Selected Abstracts

### Ectopic Pregnancy

**Logwinsky, P. N.:** Tubal Pregnancies in Our Clinic (Kiew), *Monatschr. f. Geburtsh. u. Gynäk.* 100: 25, 1935.

At the Kiew Clinic were found histories of 129 ectopic pregnancies. Inflammatory changes in the pelvic organs especially in the tubes were noted in most cases and considered to be the cause of the tubal pregnancy in most instances. The largest proportion of cases of ectopic pregnancy occurred in the ampullar portion of the tube. The best treatment for ectopic pregnancy is complete removal of the pregnant tube with excision of the uterine horn. For quick peritonealization of the raw surfaces, the round ligament may be used. Because of the infrequency of the recurrence of ectopic pregnancies and the relatively high incidence of normal conceptions after tubal pregnancies, the author believes that the nonpregnant tube should be left in place. The latter should be removed only if it shows gross abnormalities.

J. P. GREENHILL.

**Fulconis, H.:** Familial Ectopic Pregnancy, *Bull. Soc. d'obst. et de gynec.* 25: 56, 1936.

The author reports 3 cases of ectopic pregnancy occurring in two sisters and a daughter of one of them. Two of the three women were operated upon within one week. In all three cases the right tube was involved.

J. P. GREENHILL.

**Duseberg, G.:** Origin and Types of Abdominal Pregnancies, *Monatschr. f. Geburtsh. u. Gynäk.* 102: 30, 1936.

The causes of premature ectopic nidation of ova may be divided into intra- and extraovular causes. The intraovular causes consist of an abnormally large ovum, unusually rapid growth of the ovum and infections or degenerative changes in ova or sperm. The extraovular causes are divided into constitutional and acquired predispositions. Among the inherited tendencies are hypoplasia of the tubes which are therefore long and tortuous and have defective development of the tubal mucosa, anomalies of the ciliated epithelium and hypoplastic musculature. The tubes may be congenitally deformed or entirely missing. The deformities may include accessory tubes, abnormal tubal openings or tubal diverticula in any of which an ovum may become implanted. Another constitutional factor in women over forty years of age is senile involution of the tubes.

The acquired factors responsible for ectopic pregnancies are chiefly deformities of the tubes due to illness, inflammations and treatment. In addition to these malformations intra- or extratubal tumors such as polyps, fibromas, or ovarian tumors

may compress the tubal lumen or kink tubes and thus interfere with the progress of an ovum. Inflammations may produce changes both inside and outside of the tubes. While gonorrhea is the most frequent type of inflammation leading to ectopic pregnancy, others such as tuberculosis, appendicitis, abortion and puerperal infection may play a rôle.

Part of the increased frequency of tubal pregnancies is due to the increase in therapeutic and prophylactic manipulations such as curettements, the use of intra-cervical pessaries, intrauterine instillations for the purpose of producing abortions, the injection of iodized oil and contraceptive devices.

J. P. GREENHILL.

**Morillo, Luis: The Diagnostic and Prognostic Value of the Aschheim-Zondek Reaction in Extrauterine Pregnancy, Ztschr. f. Geburtsh. u. Gynäk. 110: 18, 1934.**

Morillo gives a brief résumé of 13 cases of extrauterine pregnancy proved by operation. Aschheim-Zondek tests were made in each case prior to operation. In only five cases was Reaction III positive, in only one was Reaction II positive, and in the remaining seven cases Reaction I was positive. There were no complete negative results. According to the literature Reaction III is positive in from 72 to 91 per cent of all extrauterine pregnancies. The author injected animals with extracts of chorionic tissue obtained at operation in several of the cases, and found that positive reactions could be obtained only with relatively large amounts of tissue when the pathology in the pelvis was of long standing. He therefore concludes, agreeing with other writers on the same subject, that the A-Z Reaction III is always positive early in the development of an extrauterine pregnancy, but becomes negative as the chorion loses its function through the death of the ovum. A positive Reaction III indicates that the chorion is still functioning, or that it has functioned within the past few days.

EUGENE S. AUER.

**Piraino, Amedeo, and Santomauro, Ugo: Unilateral Pupillary Dilatation as a Diagnostic Sign in Extrauterine Pregnancy, Folia gynaec.-demograph. 32: 153, 1935.**

In one-third of their cases of extrauterine pregnancy, the authors found a mydriasis of the pupil of the eye on the same side where the extrauterine pregnancy was situated. This sign may be found throughout the course of the pregnancy, and disappears only upon the surgical removal of the pregnancy, and under very deep anesthesia.

The sign although not specific should be watched for, because (1) other causes of unilateral dilatation of the pupil are easily differentiated from pregnancy; (2) the sign is present during the entire period of the extrauterine pregnancy; (3) it is an objective sign; and (4) it is easily and quickly recognized.

MARIO A. CASTALLO.

**Polowe, David: Extra-Uterine Pregnancy Following the Injection of Iodized Oil for Uterosalphingography, Am. J. Surg. 29: 244, 1935.**

Insufflation with gaseous products may successfully establish tubal patency. However, in cases of partial obstruction, such a procedure does not prevent the collapse of the tubes with the consequent reformation of intratubal adhesions as soon as such gases are absorbed (a matter of less than a day when judged by the cessation of shoulder pain). Radiopaque oils, on account of their slower absorption, therefore, may prove more successful than gases in the maintenance of tubal

patency. Here again, however, it is conceivable that inspissation or encapsulation of the oil within or about the tubes may occur and thus defeat the purpose for which it was introduced.

From the experience with the extrauterine pregnancy here reported, the author concludes that the uterotubal injection of iodized oil is not entirely harmless. It appears that the oil is not only slowly absorbed and may, by remaining in the tubes for as long as two years, retard the advent of pregnancy, but such delay in absorption may be also a factor in the development of extrauterine pregnancies. In the case here reported, it is conceivable that the oil became encapsulated at the right fimbriated end, and thus did not permit the impregnated ovum to reach its normal place of nidation within the uterus.

J. THORNWELL WITHERSPOON.

**Hoffman, A. I.: Complete Tubal Abortion From Columnar Implantation of the Ovum, Gynec. et obst. 33: 520, 1936.**

Upon the site of implantation of the ovum depends the mode of termination of a tubal pregnancy. Most frequently it terminates by tubal abortion, in which case the ovum is usually in the ampullar portion of the tube. If situated in the isthmus tubal rupture occurs.

In complete tubal abortion, which is uncommon, the entire ovum is expelled, and if there is no marked alteration of the tubal musculature the tube contracts with arrest of hemorrhage, and involution follows.

Implantation of the ovum in the ampulla may occur on the summit of a plical fold. Werth termed this "Columnar Implantation" as distinguished from "Intercolumnar Implantation" with implantation between the plicae. In the former the muscle wall remains intact or almost so for five or six weeks, particularly if the ovum succumbs early. The ovum thus suspended in the lumen of the tube by a pedicle consisting of the plica is swept by reverse peristalsis into the abdomen.

Clinically, complete tubal abortion is characterized by delay in menstruation, sudden onset of abdominal pain, and signs of internal hemorrhage and shock. From his personal experience with three patients presenting this condition the author stresses several important operative findings. There is massive peritoneal hemorrhage with the source of bleeding not apparent. The affected tube is markedly hyperemic and the ampullar portion, in contrast to the isthmus, is somewhat dilated. He suggests that the tube be gently compressed between two fingers and milked from the isthmus toward the abdominal ostium; this will express the small black blood clots that remain within the tube after complete expulsion of the ovum.

In reference to treatment he advises salpingectomy for the following reasons: (1) Hemorrhage may recur from site of detachment of ovum; (2) trophoblastic elements which are present in considerable quantity may give rise to hemorrhage as an immediate complication, or to placental mole or chorionepithelioma as a late complication; (3) the affected tube though involuted remains a potential site for another ectopic gestation.

ARNOLD GOLDBERGER.

**Paola, Guillermo Di, and Ibanez, Anibal Lemos: Bilateral Simultaneous Tubal Pregnancy, Bol. Soc. de Obst. y ginec. (Buenos Aires) 14: 837, 1936.**

The authors present a case of bilateral tubal pregnancy. They state that in the literature they could find only 4 such cases heretofore mentioned.

The theories for such an occurrence are as follows: (1) Fecundation of 2 ova from distinct follicles in the same ovary; (2) Fecundation of 2 ova from different follicles of both ovaries; (3) Fecundation of 2 ova belonging to the same follicle.

The treatment was salpingectomy, bilateral in this case, as both tubes were involved.

MARIO A. CASTALLO.

**Nandi, G. C.: Simultaneous Intra-Uterine and Extra-Uterine Pregnancy, Calcutta M. J. 29: 159, 1934.**

A case of simultaneous intra- and extrauterine pregnancy is reported. Para ii, aged twenty-five, last child fourteen years ago. Past history negative.

Last menstrual period occurred end of May, 1933. Acute pain in lower abdomen and bloody vaginal discharge started middle of July. She entered hospital, Sept. 3, 1933, complaining of pain in lower abdomen and constipation. Findings: Soft mass 2 fingers below umbilicus, toward the right side, not freely movable. Cervix soft and bulky, uterus anteverted and pushed forward by a mass attached to the uterus.

Abdominal section revealed dark blood in peritoneal cavity, a pelvic hematoma behind uterus and to left, intimately connected with corpus. Uterus was size of eight weeks' pregnancy. Left tube and ovary adherent to mass. Right appendages normal. Chorionic villi in mass and rent in left tube visible. On section uterus found to contain a fetus of eight weeks. Patient made uneventful recovery after removal of uterus and appendages.

This condition has been termed "simultaneous pregnancy," "combined pregnancy," or "compound pregnancy." It is rare since only 217 cases have been found in the literature by Gemmel and Murrey in 1933. It may be a type of twin pregnancy, one fertilized ovum implanting itself in uterus, the other in the tube; in other cases, the condition may be due to the superimposition of a uterine pregnancy upon one already existing in the tube. The latter may antedate the uterine gestation by a long or very short interval.

The literature is reviewed.

F. L. ADAIR AND S. A. PEARL.

**Kerr, J. M., and Anderson, D. F.: Angular Pregnancy. A Clinical Entity, Brit. M. J. 1: 1113, 1934.**

Author gives histories of two cases of cornual pregnancy seen in the Glasgow Royal Maternity and Women's Hospital.

Case 1, a gravida vi, fifteen weeks pregnant. Because of acute abdominal symptoms a laparotomy was performed with a provisional diagnosis of ectopic pregnancy or torsion of ovarian cyst. Exploration revealed marked elongation of the right cornu and abdomen was closed. Patient developed a pneumonia and aborted spontaneously the day following laparotomy.

Case 2, a primigravida, aged twenty-one, who before admission complained of acute abdominal cramplike pains, tenderness in right lower quadrant, tender and hard uterus. On bimanual examination a tender elongated right cornu was palpated and a diagnosis of nineteen-week angular pregnancy was made. Throughout the pregnancy she experienced these sharp pains. At thirty-five weeks gestation uterus was lying to the right side and was tender. Patient had a forceps delivery of a 5 pound 10 ounce child and uterus was explored; placenta was attached in the elongated right cornu.

Kerr discusses angular pregnancy as a particular type of gestation in which the zygote becomes implanted in one horn of the uterus and thus is distinct from the interstitial variety of ectopic. He states that he had previously observed four such cases and all six were similar in the following features: (1) Pain, (2) lateral distention of the uterus in the region of the uterine cornu, (3) tendency to abortion. Three of six cases ended in abortion.



Since it attracts attention between twelfth and twentieth weeks of gestation, it should be differentiated from ectopic pregnancy, pregnancy in a rudimentary horn, fibromyomas undergoing degeneration, torsion of the pedicle of an ovarian cyst, appendicitis with lateral flexion of the uterus and finally, pyelitis with pregnancy.

F. L. ADAIR AND S. J. BENENSOHN.

**Guillemin, A.: Peritoneal Hemorrhage From a Ruptured Ovarian Follicle, Soc. d'obst. et gynec. 25: 497, 1936.**

A young girl was operated upon because of a severe intraabdominal hemorrhage as a result of rupture of a corpus luteum. The author removed the involved ovary. This operation was performed March 21, 1935, when the patient was sixteen years old. On Jan. 26, 1936, she had a second laparotomy for a similar condition on the opposite side. The second ovary was removed but the author transplanted a portion of it under the skin. The first hemorrhage resulted four days before the expected menstrual period, while the second one appeared fifteen days after the last menstrual period.

J. P. GREENHILL.

**Tomasi, Luigi: Primary Abdominal Pregnancy, Clin. ostet. (Bari) 37: 404, 1935.**

The author describes a case in which the physical examination revealed all the classical symptoms of a ruptured tubal pregnancy, while during laparotomy the uterus and fallopian tubes were found to be normal. The source of the imposing hemorrhage was a hemorrhagic tumor situated on the anterior surface of the rectum.

He maintains that this was a case of true primary abdominal pregnancy.

AUGUST F. DARO.

**Costa, Nicanor Palacios, and Falsia, Antonio: Ovarian Pregnancy, Bol. Soc. de obst. y ginec. (Buenos Aires) 14: 126, 1936.**

A patient with an ovarian pregnancy is reported. The preoperative diagnosis was ectopic pregnancy. Histologic slides are shown to prove the correctness of the diagnosis.

MARIO A. CASTALLO.

**Fox, E. A.: Extrauterine Pregnancy Partially Eliminated Through the Intestinal Tract, Bol. Soc. de obst. y ginec. (Buenos Aires) 14: 121, 1935.**

The author reports the history of a forty-one-year-old multipara with undiagnosed abdominal pathology on admission to the hospital. During observation period the patient passed a fetal tibia and clavicle while defecating.

Roentgenography disclosed a fetal skull in the pelvis, which was found to be in the large intestine at operation for its removal through the abdominal route. Uneventful recovery.

MARIO A. CASTALLO.

**Hosking, Archer: Abdominal Delivery of 254-Day Extrauterine Foetus, Brit. M. J. 2: 111, 1934.**

The author describes the removal of a fetus from the abdomen by laparotomy at 254 days. The operation was exceedingly simple. The placenta had remained completely within the tube, and the absence of adhesions was remarkably favorable.

The patient, aged 35, had had an ectopic pregnancy three years previously at seven weeks' pregnancy, followed by removal of the right tube. No other preg-

nancies occurred until the present. Constipation and lower abdominal pain were present throughout pregnancy.

The baby weighing 5 pounds 12 ounces survived nine hours. The mother recovered after a complicated puerperium of seven weeks. Normal menstruation was established three months after operation.

F. L. ADAIR AND S. A. PEARL.

**Krishnan, R. G.: Full-Term Extrauterine Pregnancy: Child Delivered Alive,** Brit. M. J. 1: 795, 1936.

The record is given of a full-term extrauterine pregnancy in a para vii, aged thirty-three, delivered of a live child by laparotomy. The placenta lodged in the layers of the left broad ligament and the amniotic cavity was firmly enclosed by adhesions. The uterus appeared to be the size of a twelve weeks' gestation. Pain during pregnancy and slight periodic vaginal bleeding occurred. Recovery was uneventful.

F. L. ADAIR AND S. A. PEARL.

**Steel, W. Arklay: Full-Term Extrauterine Pregnancy With Living Child,** Brit. M. J. 2: 62, 1934.

Primipara, aged twenty-four, with a ventral hernia due to an appendicitis operation scar. Complained of very severe "knifelike" pains. Temperature, pulse, and urine were normal. There was marked tenderness over the entire abdomen. The cervix was soft and the external os closed. The fetus was found lying transverse. An external version was attempted, when a "snap" was felt and then a large placenta made out, occupying the entire pelvis. The patient became shocked. The uterus was thought to be ruptured and a laparotomy done. A living female child was extracted from the abdominal cavity which was filled with blood. The uterus was anterior to the placenta. The placenta was attached by a broad pedicle (3 to 4 inches) to the posterior aspect of the right broad ligament. A pint of blood sucked out of the peritoneal cavity was given to her intravenously. She rapidly improved, showing the value of auto-transfusion. The child seemed healthy but died suddenly twelve hours after birth. Autopsy on the child showed nothing abnormal.

F. L. ADAIR AND I. BROWN.

**Tallaferro, Federico: A Case of Extrauterine Pregnancy at Term,** Bol. Soc. de obst. y ginec. (Buenos Aires) 15: 411, 1936.

The author reports a case of extrauterine pregnancy at term. The case was diagnosed by x-ray after injection into the uterus of a radiopaque substance. A live child was obtained by means of abdominal operation. Most of the placenta was left in situ, with drainage through Douglas' pouch. The patient finally died from peritonitis.

MARIO A. CASTALLO.

## Books Received

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**INTIMATE SIDE OF A WOMAN'S LIFE.** By Leona W. Chalmers. Illustrated, 128 pages. Pioneer Publications, Inc., Radio City, N. Y., 1937.

**PHYSICIANS' GUIDE BOOK for Mothers.** By G. G. Keener, M.D. Southern Publishers, Inc., Kingsport, Tenn., 1936.

**SAFE CHILDBIRTH.** The Three Essentials. By Kathleen Olga Vaughan, formerly medical officer, Egyptian Quarantine, etc. With foreword by Howard A. Kelly. Illustrated, 154 pages. William Wood and Company, Baltimore, 1937.

**DISEASES OF INFANTS AND CHILDREN.** By J. P. Crozer Griffith, M.D., Emeritus Professor of Pediatrics in the University of Pennsylvania, etc., and A. Graeme Mitchell, M.D., Professor of Pediatrics, College of Medicine, University of Cincinnati, etc. Second edition, revised and reset. Illustrated, 1154 pages. W. B. Saunders Company, Philadelphia, 1937.

**PREOPERATIVE AND POSTOPERATIVE TREATMENT.** By Robert L. Mason, M. D., assistant in surgery of the Massachusetts General Hospital. Illustrated, 495 pages. W. B. Saunders Company, Philadelphia, 1937.

**KAMA SUTRA**, the Hindu Science of Love. Translated from the Sanscrit by Sir Richard Burton. Illustrated, 127 pages. The Medical Press of New York, New York, 1936.

**DAS HORMON DES CORPUS LUTEUM.** Von Dr. Erich Fels, Instituto de Maternidad de la Sociedad de Beneficencia, Buenos Aires. Mit 40 Abbildungen im Text, 169 Seiten. Franz Deuticke, Wien, 1937.

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## Item

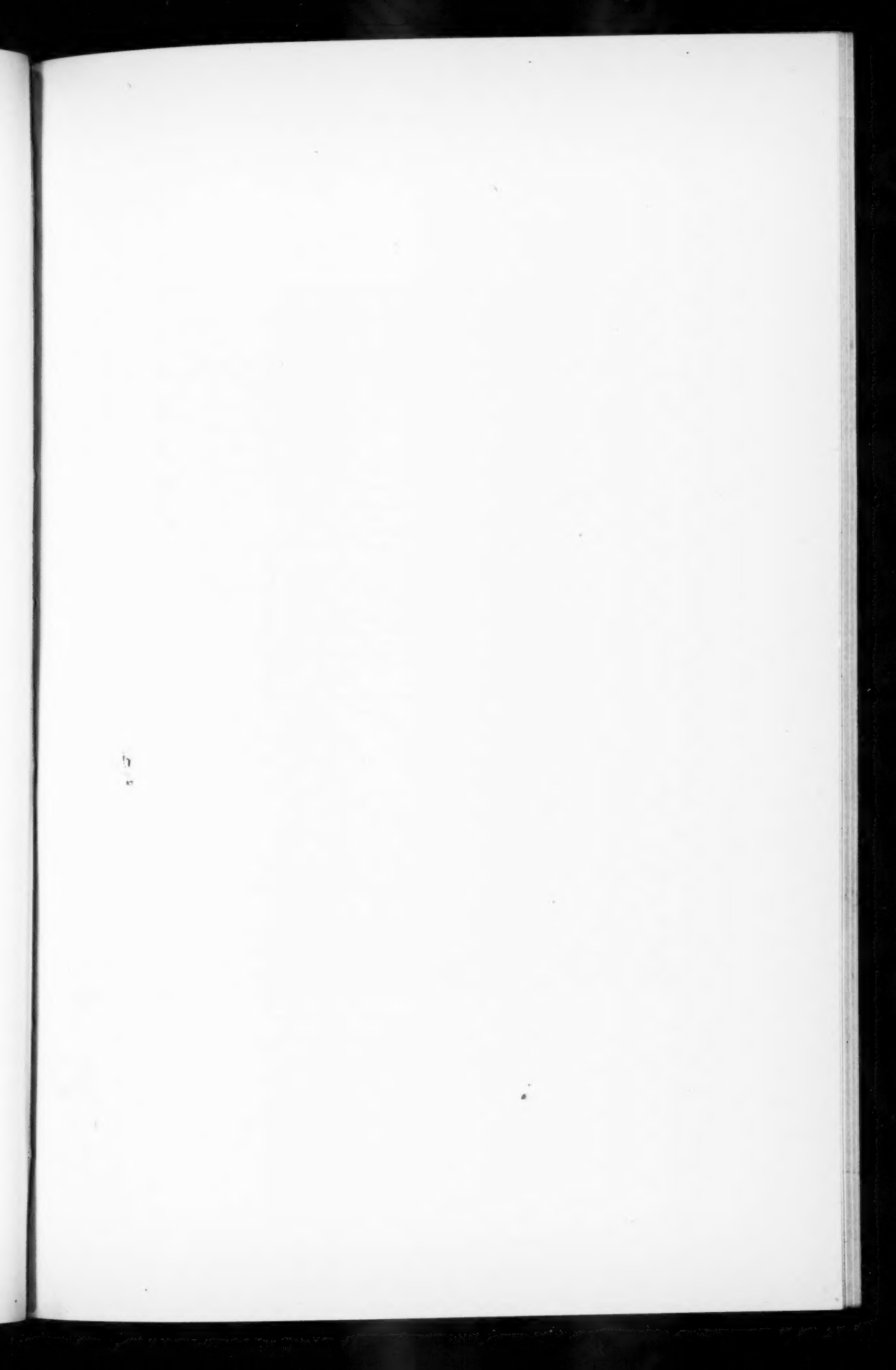
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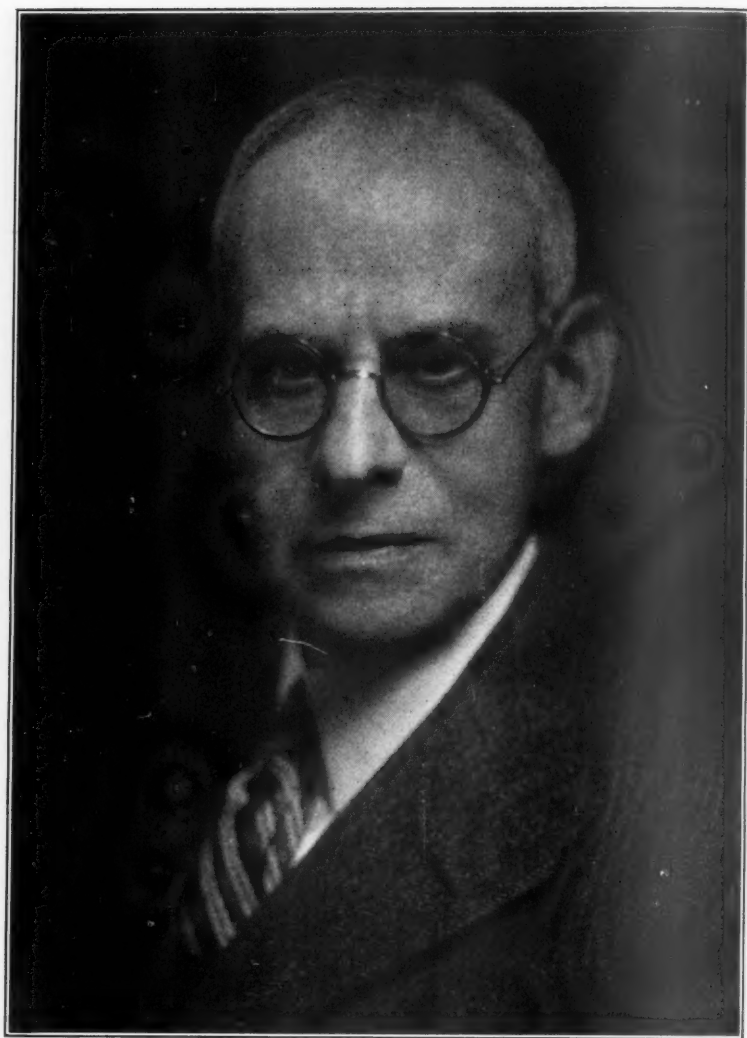
### American Board of Obstetrics and Gynecology

Practical oral-clinical, and pathological examinations for Group A and Group B applicants will be held at Atlantic City, N. J., on June 7 and 8, 1937.

An informal dinner for the Diplomates of this Board and others interested in obstetrics and gynecology will be held at the Hotel Claridge, Atlantic City, on Wednesday, June 9, 1937, at 7:00 P.M. At this time several short addresses will be made and the successful candidates of the preceding two days' examinations will be introduced in person.

Applications for the Group A examination will be received in the office of the Secretary, Dr. Paul Titus, 1015 Highland Building, Pittsburgh (6), Pa., to April 9, 1937. Application blanks may be secured from the Secretary's office.





*Robert T. Hank*